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BRAIN.

PART I., 1899.

Original Articles and Clinical Cases.

ON THE LOCALISATION OF INTRACRANIAL TUMOURS.[1]

BY BYROM BRAMWELL, M.D.

At a discussion on Intra-cranial Surgery at the Edinburgh Medico-Chirurgical Society a few years ago (February 21, 1894), I analysed all the cases of intracranial tumour—82 in number—which had been under my own care up to that time. Since being invited to take part in the discussion, I have carefully gone over the notes of these cases, weeding out a few cases in which the diagnosis was perhaps doubtful, and adding the additional cases which have since come under my notice.

The *total number* of cases of intracranial tumour which have been under my own care during life up to the present time is 122.

The *results* in these 122 cases were as follows :—

Fatal :—		
(*a*) With *post-mortem* examination	40	
(*b*) Without *post-mortem* examination	36	
	— ...	76
Cured or apparently cured :—		
(*a*) Non-syphilitic cases (some of them were perhaps cases of distended ventricles and not tumours)	4	
(*b*) Syphilitic cases	7	
	— ...	11

---

[1] Being a contribution to the discussion on Tumours, published in BRAIN, 1898, p. 291.

Greatly relieved :[1]—		
(*a*) Non-syphilitic cases	1	
(*b*) Syphilitic cases	10	
	—	... 11
Remaining in statu quo :—		
(*a*) Non-syphilitic cases	12	
(*b*) Syphilitic cases	1	... 13
Result unknown :—	11	
	—	.. 11
		—
Total		... 122

In this discussion I shall only, of course, refer to the cases in which the exact localisation of the tumour was definitely ascertained by *post-mortem* examination, and to two cases, in one of which the position of the tumour was verified, and in the other not verified by operative procedure.

In the following table, the position and nature of the tumour in the 40 cases which were verified by *post-mortem* examination are shown:—

Table showing Position and Nature of the Tumour in 40 Cases of Intracranial Tumour under Dr. Byrom Bramwell's care during life, and examined Post mortem.

No.	Age.	Sex.	Position of Tumour.	Nature of Tumour.
1	41	M.	Right angular gyrus and adjacent parts of the parietal and occipital lobes.	Syphilitic.
2	40	M.	Right frontal lobe, first convolution and subjacent white matter.	Glioma and cyst.
3	45	M.	Left frontal lobe, first convolution and subjacent white matter.	Lympho - sarcomatous cyst.
4	64	F.	Left lateral lobe of the cerebellum.	Sarcoma of the membranes.
5	34	M.	Right frontal lobe, first and second convolutions and subjacent white matter.	Syphilitic.
6	20	F.	Right motor area and second and third frontal convolutions, island of Reil, and tip of temporo-sphenoidal lobe.	Sarcoma of the membranes.
7	5	M.	Six tumours: (1) first left frontal convolution; (2) tip of left occipital lobe; (3) right gyrus fornicatus: (4) left gyrus fornicatus; (5) right angular gyrus; (6) head of left corpus striatum.	Tubercular.
8	9	F.	Cerebellum, right lateral lobe.	Tubercular.
9	34	M.	Right motor area.	Secondary cancer.

---

[1] In several of these cases the ultimate result is not known.

No.	Age.	Sex.	Position of Tumour	Nature of Tumour.
10	1½	F.	Left crus and cerebellum.	Tubercular
11	60	M	Left occipital lobe.	Syphilitic.
12	4	M	Vertex.	Perforating sarcoma.
13	50	M	Right optic thalamus.	Glio-sarcoma.
14	39	M	Motor area and subcortical white matter.	Glio-sarcoma.
15	18	M	Cerebellum: four tumours—three in the left and one in the right lateral lobe.	Tubercular.
16	34	F.	Right side of pons.	Glio-sarcoma.
17	34	F.	Second left frontal convolution.	Glio-sarcoma.
18	63	F	Left centrum ovale, just behind motor area and right island of Reil, and right lenticular nucleus.	Glio-sarcoma.
19	29	F	Left motor area and posterior end of the third left frontal convolution, and the subjacent white matter.	Glioma with cyst.
20	54	M.	Right arm centre	Glioma.
21	28	F.	Pons.	Glioma.
22	32	M.	Left frontal, temporo-sphenoidal and occipital lobes.	Glioma and cyst.
23	45	M.	Right centrum ovale, internal capsule and optic thalamus.	Glioma.
24	24	M.	Cerebellum, middle and right lateral lobes.	Glioma and cyst.
25	47	F.	Vertex.	Cancer of membranes.
26	47	F.	Left frontal lobe	Glioma and cyst.
27	24	M	Cerebellum, left lateral and middle lobes.	Glioma.
28	30	M.	Left centrum ovale and motor area.	Glioma.
29	17	F.	Cerebellum, middle and right lateral lobes.	Glioma.
30	51	F.	Base, pressing on left side of pons.	Fibro-sarcoma of membranes.
31	61	F.	Cerebellum, right lateral lobe, left lenticular nucleus and right ascending parietal convolution.	Secondary cancer.
32	26	F.	Left occipital cortex, etc.	Melanotic sarcoma.
33	21	F.	Pituitary body.	Sarcoma.
34	26	M	Left centrum ovale.	Large glioma.
35	52	M	Left frontal lobe.	Glioma.
36	40	M	Base, right side of pons.	Fibro-sarcoma.
37	57	M.	Right temporo-sphenoidal lobe and second right frontal convolution.	Glioma and cyst.
38	8	F.	Left crus.	Tubercular.
39	42	M.	Left parietal lobe. Also large abscess in subjacent white matter.	Fibro-cellular.
40	7½	F	Right side of pons, right crus and cerebellum.	Glioma.

On analysing this table I find that the position of the tumour in the 40 fatal cases which were examined *post mortem* was as follows:—

Frontal Lobe.—In six cases the tumour was confined to the frontal lobe (viz., 2, 3, 5, 17, 26 and 35).

In five other cases (viz., 6, 7, 19, 22 and 37) the frontal lobe was involved in addition to other parts.

Island of Reil.—In three cases (18, 19 and 22) the tumour involved the island of Reil; in all of these cases other parts were also involved.

Motor Area and Subcortical Motor Tracts.—In ten cases the tumour was situated in the motor area or subcortical tissues immediately below the motor area (viz., 6, 9, 14, 18, 19, 20, 23, 25, 28 and 34). In several of these cases other parts (frontal lobe, &c.) were also involved.

Tempero-Sphenoidal Lobe.—In two cases (viz., 22 and 37) the tumour was situated in the temporo-sphenoidal lobe; in both of these cases other parts were also involved.

Occipital Lobe.—In one case (11) the lesion (a healed syphilitic gumma) was limited to the occipital lobe; and in three cases (7, 22 and 28) the occipital lobe was involved as well as other parts.

Parietal Lobe.—In two cases (viz., 1 and 39) the tumour was situated in the parietal lobe.

Basal Ganglia. (*a*) *Optic Thalamus.*—In one case (13) the tumour had its primary seat in the right optic thalamus. In three other cases (22, 23 and 32) the optic thalamus was involved along with other parts.

(*b*) *Lenticular Nucleus.*—In two cases (18 and 31) the lenticular nucleus was involved along with other parts.

(*c*) *Caudate Nucleus.*—In two cases (7 and 18) the caudate nucleus was involved along with other parts.

Base of the Brain.—In three cases (30, 33 and 36) the tumour was situated at the base of the brain outside the nervous tissues.

In one of these cases (33) the tumour affected the *pituitary body.*

Crus Cerebri.—In two cases (10 and 33) the tumour was situated in the crus cerebri.

Pons Varolii.—In three cases (16, 21 and 40) the tumour was situated in the pons. In two other cases (30 and 36) the pons was implicated by tumours which had their primary seat outside the nervous tissues.

Cerebellum.—In seven cases (4, 8, 15, 24, 27, 29 and 31) the tumour was situated in the cerebellum. In three other cases (10, 32 and 40) the cerebellum was also involved by a tumour, either springing from the membranes, or a tumour which involved other parts of the nervous tissues as well as the cerebellum.

Various Situations.—In two cases (7 and 32) the tumour or tumours involved a number of different parts of the cerebral and cerebellar tissues.

In one case (12) the tumour (a perforating sarcoma of the skull) involved the outer surface of the dura mater in the frontal and vertical regions and the frontal and parietal bones.

The primary seat of the tumour in the 40 cases was therefore as follows :—

	CASES
Frontal lobe	6
Motor area	10
Temporo-sphenoidal lobe	2
Occipital lobe	1
Parietal lobe	2
Optic thalamus	1
Base (extra nervous)	3
Crus cerebri	2
Pons Varolii	3
Cerebellum	7
Various positions	2
Extradural (perforating sarcoma of the skull) ...	1
Total ...	40

The number of cases included in any one group is too small to warrant generalised conclusions, especially since some of the cases were seen twenty-four years ago; but many of the individual cases afford important information as to the positive (localising) symptoms and as to the negative symptoms which may result from the presence of a tumour in the special parts of the brain and cerebellum which are included in this discussion. (I shall only, of course, refer to tumours in the frontal, temporo-sphenoidal and occipital lobes, the basal ganglia and the cerebellum, since tumours involving the motor area and the subjacent white matter, and tumours of the base, pituitary body, crus cerebri, pons Varolii and medulla oblongata are not included in this discussion.)

I propose, then, to detail briefly the more important clinical features of some of the individual cases, pointing out the positive and negative facts of localising value which they exhibit. The negative facts are in many instances very striking; and, from a diagnostic point of view, are, of course, as important as the positive localising symptoms. Speaking generally, I may say that as my experience of intracranial tumours increases I become more and more cautious in drawing conclusions from the clinical data as to the exact position of the new growth. I have met with cases in which an intracranial tumour has been situated in every one of the parts of the cerebrum which are specially included in this discussion, and in the cerebellum, in which there were absolutely no localising symptoms indicative of the position of the tumour. I make one exception only, for when the occipital lobe is the seat of the tumour (*i.e.*, when the half-vision centre or the optic radiations of Gratiolet are implicated by the tumour), hemianopsia is probably always present. But I speak tentatively on this point, for I have seen very few tumours of the occipital lobe.

In two cases (4 and 39) a tumour was found after death, the presence of which was entirely unsuspected during life, *i.e.*, in both cases the tumour seemed to be entirely "latent."

TUMOURS OF THE FRONTAL LOBE.

In six cases the tumour was limited to the frontal lobe, and in five other cases the frontal lobe was involved along with other parts. The more important features of the six cases in which the tumour was confined to the frontal lobe were as follows:—

(*A.*) CASES IN WHICH THE TUMOUR WAS LIMITED TO THE FRONTAL LOBE.

Case I. (Case 2 in the Table). *Glioma and cyst of the right frontal lobe involving the middle part of the first frontal convolution and the subjacent white matter.*

D. M., aged 40, pitman, admitted to the Newcastle-on-Tyne Infirmary on March 22, 1875.

A. General Symptoms. Headache (intense and usually frontal); vomiting (frequent and severe); giddiness; optic neuritis (intense, limited to the left eye, the right eye having been previously destroyed by an injury); several severe general epileptic fits.

B. Localising Symptoms. (*a*) *Mental Symptoms.* There is a marked change in the patient's mental condition; he has a silly expression; is at times irritable, obstinate and passionate, at other times depressed and stupid; his memory is markedly impaired; he frequently bursts into meaningless laughter; he sleeps well, but while sleeping grinds his teeth. Soon after his admission to hospital he developed delusions of suspicion and had to be sent to an asylum.

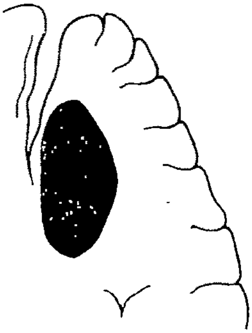

FIG. 1.

Section through the right frontal lobe of the brain in the case of D. M. (Case 1), showing the position of the lesion.

(*b*) *Motor Functions.* The gait is peculiar, he takes a few quick steps to the left, then a few quick steps to the right, often breaking into a short run; he frequently has attacks of temporary loss of power in the left side, occasionally in the right side; he every now and again falls, apparently from sudden loss of power in the left leg.

The *knee-jerks* were not examined; the *plantar reflex* was more marked on the left than on the right side.

(*c*) *Speech.* No aphasic symptoms.

(*d*) *Pseudo-localising Symptoms.* A cicatrix, the result of a severe head injury received a year ago, is present 2½ inches above and slightly behind the left ear; he was quite well until this injury; the head symptoms developed immediately after the injury. Perhaps the tumour developed at the point of *contre-coup.*

Result. He became comatose on September 18, 1875, and died on September 20.

Post-mortem. Intra-cranial pressure greatly increased; Pacchionian bodies very prominent and had eroded the skull; convolutions flattened and sulci effaced; ventricles somewhat dilated; a gliomatous tumour and cyst in the right frontal lobe, involving the upper frontal convolution and the subjacent white matter (see fig. 1). Brain otherwise quite normal; weight, 59 ounces (cerebrum, 50½; cerebellum, 8½ ounces).

Remarks. In this case mental symptoms were very marked; and temporary paralysis, usually on the opposite side, sometimes in *both* legs, frequently recurred; the gait was peculiar; grinding of the teeth also occurred.

Case 2 (Case 3 in Table). *Glioma and cyst of the left frontal lobe, involving the middle part of the first frontal convolution and the subjacent white matter.*

W. A., aged 45, pitman, admitted to the Newcastle-on-Tyne Infirmary on October 1, 1894, suffering from an intra-thoracic tumour and head symptoms. The case was a very interesting and complicated one; the head symptoms were as follows:—

General Symptoms. No headache, vomiting, or giddiness mentioned in the notes; optic discs not examined; no fits.

Mental Symptoms. A marked change in patient's mental condition; is irritable and obstinate, will sit silent for hours and only answers questions in monosyllables; sleeps badly and often grinds his teeth.

Speech. Distinct motor aphasia.

Motor Functions. Right hemiplegia, which varied *greatly* in its degree from time to time.

Knee-jerks not examined.

Result. The mental symptoms and the paralysis varied considerably from day to day. A few days before death the right-sided hemiplegia, which the day previously had almost passed off, *suddenly* became complete, diarrhœa developed, the temperature rose to 102°, and the patient died November 6, 1894.

Post-mortem Appearances. Large lympho-sarcoma in thorax; pericarditis; secondary lympho-sarcomatous deposits in the abdominal and mesenteric glands, the left suprarenal capsule and the small intestine; lympho-sarcomatous cyst the size of a hen's egg in the left frontal lobe, involving the middle part of the first frontal convolution and the subjacent white matter (see fig. 2); a quite recent embolus in the left middle cerebral artery (apparently this was the cause of the complete hemiplegia which developed suddenly a few days before death).

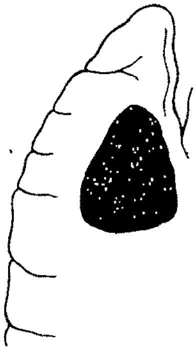

FIG. 2

Section through the left frontal lobe of the brain in the case of W. A. (Case 2), showing the position of the lesion.

Remarks. In this case mental symptoms were very marked; right hemiplegia very variable in degree and some motor aphasia seemed to be caused by the tumour; grinding of the teeth also occurred.

Case 3. (Case 5 in Table). *Syphilitic tumour involving the posterior end of the 1st and 2nd right frontal convolutions and the subjacent white matter and irritating the adjacent part of the motor cortex.*

J. M., aged 34, bricklayer, admitted to the Newcastle-on-Tyne Infirmary on November 4, 1875, suffering from left hemiplegia and Jacksonian epilepsy.

Previous History. Syphilis seven years previously. For two years "rheumatic" pains, worse at night; several attacks of severe headache. Seven weeks ago, a severe, general epileptic fit; two weeks ago, a second fit, unattended with loss of consciousness, limited to the left side and followed by left hemiplegia.

General Symptoms. Headache (severe, frontal and vertical); double optic neuritis, intense in degree.

Mental Symptoms. Mental condition very much impaired, all the mental processes being markedly blurred.

Speech. No aphasia.

Motor Functions. Left hemiplegia, involving the face, arm and leg, following Jacksonian epilepsy, which involved the left side of the body, and which had occurred a fortnight previously.

Knee-jerks not examined; *plantar reflex* more marked on the right (non-paralysed) side.

Immediate Result. Under anti-syphilitic treatment the patient made an excellent recovery and was discharged quite well on January 31, 1876.

Subsequent Progress. On September 23, 1876, he fell from a high scaffold, fractured his clavicle and received a severe cut on the right side of his head; was confined to bed for a month, suffering from severe headache; then returned to work.

On *February* 9, 1877, was seized with Jacksonian epilepsy; the fits continued to recur with great regularity and frequency; was re-admitted to the Newcastle-on-Tyne Infirmary on February 23, 1877, suffering from left hemiplegia and frequently recurring attacks of Jacksonian epilepsy; the spasms commenced with drawing up of *both* legs and chiefly affected the left side of the body; it was calculated that the patient had 4,320 fits.

Under treatment rapid improvement occurred, and the patient was discharged, well, on April 20, 1877.

He continued to follow his employment, and so far as could be ascertained made no complaint until December 31, 1877, when he was seized with a severe general epileptic fit, followed by coma and death.

Post-mortem Appearances. The scalp and skull-cap were natural; the dura was firmly adherent over a circumscribed spot corresponding to the posterior end of the second right frontal convolution. The surface of the brain at the point of adhesion was depressed, and on cutting into it this was found to be due to the contraction of a new growth (syphilitic gumma). The tumour involved the posterior end of the first and second right frontal convolutions and the subjacent white matter (see fig. 3); it did not directly involve the adjacent motor cortex (ascending frontal convolution).

Remarks. In this case the frequently recurring attacks of Jacksonian epilepsy, which commenced with drawing up

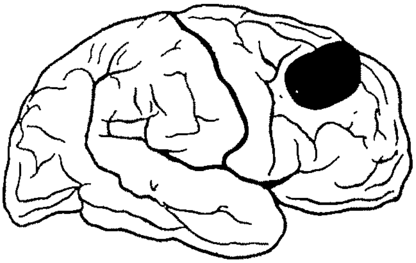

FIG. 8.

Right hemisphere of the brain in the case of J. M. (Case 8), showing the position of the lesion.

of *both* legs, suggested that the tumour was situated in the motor area (leg centre, or involving both leg centres at the vertex); the tumour involved the second right frontal convolution and its subjacent white matter; it had no doubt irritated the adjacent part of the motor area, but that was the arm centre.

Case 4. (Case 17 in Table). *Two sarcomatous tumours of the left frontal lobe; one small (the size of a Spanish olive) in the tip; the other large (the size of a large egg) was limited to, and had produced complete destruction of, the posterior end of the second left frontal convolution; no localising symptoms; no agraphia.*

J. S., aged 34, widow, admitted to the Edinburgh Royal Infirmary on February 15, 1896, suffering from headache, vomiting and dimness of vision.

Duration. The headache commenced a year ago; five months ago the patient experienced a tingling sensation all over the body (resembling that of the foot being asleep) and then vomited; has continued to vomit occasionally since; five weeks ago she noticed that her sight was becoming dim.

General Symptoms. Headache (very severe, occipital and frontal, continuous, with exacerbations, for the past five months); vomiting (occurs usually with exacerbations of the headache, generally before breakfast); dimness of vision in the left eye; giddiness and an occasional tendency to fall backwards when walking; a prickling sensation in the eyes; double vision;

double optic neuritis, more marked in the left than in the right eye, but moderate in degree even in the left eye.

Mental Symptoms. Absolutely none; the patient is intelligent and well educated, extremely bright and active mentally.

Speech. No aphasic defect of any kind; in particular, no agraphia.

Motor Functions. Slight paralysis of the left external rectus muscle and associated nystagmus in the right eye when the patient attempts to look right out to the left.

Knee-jerks equal and normal in degree.

Diagnosis. An intracranial tumour; position uncertain, but probably in the left hemisphere, because of the paralysis of the left external rectus.

Progress of the Case. During her stay in hospital the patient continued to have very severe headache and frequent attacks of vomiting.

On March 12, 1896, she complained of feeling dull and heavy; the optic neuritis was more marked.

On March 18, 1896, was discharged at her own request.

On June 1, 1896, was re-admitted; eyesight worse, optic neuritis more marked; headache intense, chiefly frontal; vomiting frequent and severe; giddiness frequent. Attacks of pain and a prickling feeling in the left side of the lips, tongue, roof of the mouth and left side of the face, never affecting the right side of these parts; occurring in paroxysms of some hours' duration; a numb feeling on the left side of the face, but no discoverable anæsthesia; the slightest touch is felt on the left side of the face, but the patient says the sensation produced by a slight touch is "awful different" from that produced by a corresponding touch on the right side. Occasional jerkings of both hands and arms, with a feeling of weakness in the legs and a sensation of nausea; these attacks occur in paroxysms of about five minutes' duration. Optic neuritis more marked. No mental or aphasic symptoms. The paralysis of the left external rectus *in statu quo.*

Knee-jerks equal and normal in degree.

June 9, 1896. Had an attack of jerkings affecting both arms and both legs and lasting for five minutes. The spasm commenced in the right leg.

June 10, 1896. Had an extremely severe attack of frontal headache; it developed suddenly, was attended with great restlessness and excitement, and was followed by extreme exhaustion; was only relieved by a hypodermic injection of morphia.

Several attacks of a similar nature, all requiring morphia for their relief, occurred during the next week.

June 17, 1896. Had an attack of clonic spasms (Jacksonian epilepsy) affecting the *left* foot and leg muscles.

June 22 *and* 26, 1896. Attacks of clonic spasms affecting both arms and both legs and the *left* side of the face.

June 30 *and July* 4. Attacks of intense headache, followed by great exhaustion; relieved by morphia hypodermically. These attacks were so alarming that palliative trephining (for the relief of the headache) was decided upon.

Up to this time, there had been absolutely no mental symptoms, no aphasic symptoms, in particular no agraphia.

The *operation* was performed by Mr. Cotterill on July 7, 1896, the trephine opening being made over the right motor area, since on June 17 the clonic spasms had been limited to the *left* foot and leg, though, in the earlier stages of the case, I was on the whole inclined to think that the tumour was probably situated on the right side. On opening the dura the intra-cranial pressure was found to be increased; nothing else abnormal was seen.

The operation was followed by great relief as regards the headache, but left hemiplegia and a condition of partial dementia unfortunately developed, evidently due to cerebritis.

The patient was re-admitted to my ward some three months later completely hemiplegic on the left side, and in a condition of marked mental enfeeblement. During the next two months there was some slight improvement.

On December 21, 1896, she was sent to the Rosslynlee Asylum. I am indebted to the Superintendent, Dr. Mitchell, and to his Assistant, Dr. Cross, for the following notes of her condition:—

On admission she was suffering from left hemiplegia and mental enfeeblement, and she was facile and emotional.

On February 1, 1897, she was better, talking sensibly, and very grateful for what was done for her.

On March 4, 1897, sensible and cheerful. Dr. Mitchell at this date wrote me:—"I cannot detect much wrong with her mentally, except mild enfeeblement and emotionalism."

During April, 1897, she became worse; her articulation and voice were much weaker; it was doubtful if she correctly understood what was said to her; her condition was that of dementia. She died on *May* 22, 1897.

On post-mortem examination the membranes were adherent over the right motor area (the position of the trephine wound); the subjacent cortical and sub-cortical tissues were sclerosed—in a cicatricial condition, the result of meningo-cerebritis.

Two sarcomatous tumours were present in the left frontal lobe, viz.:—One of small size (the size of a Spanish olive) in the very tip. Another of large size (fully the size of a hen's egg) had replaced and entirely destroyed the posterior third of the second left frontal convolution (see fig. 4); the posterior end of the first left frontal convolution and the adjacent part of the left ascending frontal convolution were encroached upon but not destroyed; the third left frontal convolution did not appear to be involved.

The brain was otherwise normal. Dr. Cross, the Assistant Medical Officer to the Asylum, kindly brought the brain to me after the *post-mortem* examination, and I personally verified the exact localisation, as described and depicted by him.

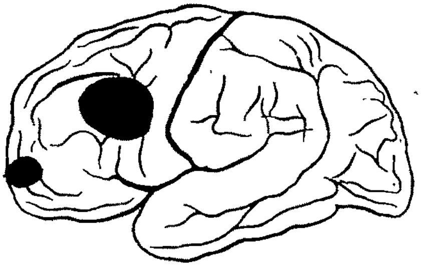

FIG. 4.

Left hemisphere of the brain in the case of J. S. (Case 4), showing the position of the tumours.

Remarks.—In this case, in which the posterior third of the second left frontal convolution (Exner's writing-speech centre) was entirely destroyed, there were, up to the time of the operation, absolutely no mental symptoms and no agraphia. While the patient was in hospital, she was in the habit of writing to her friends, and they state that there was absolutely no defect in her writing or in her power of expressing herself in writing. After the operation she did not write any letters (owing to the enfeebled mental condition), but she was able to write. While she was in the Rosslynlee Asylum, she gave instructions for her will, and wrote with her own hand, "Please give my father-in-law M—— B——, my money," and signed this document.

In this case there were no symptoms indicative of the position of a tumour in the left frontal lobe. The following pseudo-localising symptoms (suggestive of a lesion in other parts of the brain) were observed during the course of the case:—A tendency to fall backwards; slight paralysis of the left external rectus muscle (probably due to indirect pressure on the left 6th nerve); a prickling feeling in the *left* side of the lips, tongue, roof of the mouth and face; occasional jerkings of *both* legs; localised clonic spasms affecting the muscles of the *left* foot and leg; spasmodic twitchings of the *left* side of the face.

Case 5. (Case 26 in Table). *Large glio-sarcomatous tumour and cyst of the left frontal lobe, involving and destroying the anterior two-thirds of the first and second and the anterior half of the third left frontal convolution and the subjacent white matter; the posterior third of the first and second and the greater part of the posterior end of the third left frontal convolutions and their subjacent white matter were softened, œdematous and to some extent infiltrated, though not completely destroyed by the new growth.*

A. B., female, single, aged 47, was seen with Dr. Foulis on October 16, 1884, complaining of headache, vomiting and partial loss of power in the right arm and leg.

Previous History.—At the age of 12 years, suffered from "brain fever"; at the age of 37, had an epileptic fit, after which a distinct and permanent change in her mental condition was noticed; at the age of 45, ceased to menstruate, and immediately after this the cerebral symptoms for which I saw her began to develop.

General Symptoms.—Headache (very severe, at first in the area of distribution of the left great occipital nerve, afterwards in the left frontal and parietal regions); vomiting; pseudo-apoplectic attacks (in which the patient would sleep for twenty-four hours at a time), attended with pyrexia (in one of them the temperature rose to 105°); no optic neuritis (though Dr. Thomas Barlow, who had seen the patient some months previously, had found slight optic neuritis in the left eye).

Mental Symptoms.—Vacant expression; loss of the power of attention and mental concentration, a dazed condition at times; impairment of memory; at times incoherent and rambling in her talk.

Condition of Speech.—Temporary attacks of partial motor aphasia, with the use of wrong words.

Motor Symptoms.—Partial loss of power in the right arm and leg; tongue protruded to the right; a tendency of the head to fall to the right side.

Knee-jerks.—The right very feeble, left active. *Plantar reflex* active on both sides.

Pseudo-localising Symptoms.—Neuralgic pains in the area of distribution of the left great occipital nerve, temporary double facial paralysis (observed by Dr. Foulis), marked difficulty in swallowing; difficulty in articulation. (These symptoms were suggestive of a lesion in the region of the pons Varolii. Dr. Barlow had also thought that the symptoms, when he saw the patient, were indicative of a lesion "far back.")

Subsequent Progress.—Severe left-sided headache, chiefly frontal and occipital; frequent vomiting, difficulty in mastication, difficulty in swallowing, violent coughing (due apparently to "crumbs going the wrong way" and suggestive of paralysis of the larynx); answers questions in whispers only; ultimately complete right-sided hemiplegia and marked motor aphasia.

Death.—March 19, 1885.

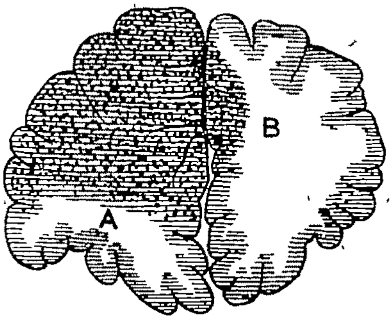

FIG. 5.

Section through the frontal lobes of the brain in the case of A. B. (Case 5), showing the position of the lesion.

The letter *A* points to the lesion in the left frontal lobe.

The letter *B* points to a portion of the right frontal lobe affected by the direct extension of the tumour.

Post-mortem Examination.—No general increase of intracranial pressure, left frontal lobe markedly larger than the right, the dura adherent over the left frontal lobe; a large gliosarcomatous tumour with a cyst the size of a hen's egg in the left frontal lobe, involving the parts already described in the heading of the case (see fig. 5).

Brain otherwise quite normal.

Remarks. In this case, in which the tumour was situated in the left frontal lobe, the following pseudo-localising symptoms were noted:—Neuralgic pains in the area of distribution of the left great occipital nerve; temporary double facial paralysis (observed by Dr. Foulis); difficulty in mastication; marked difficulty in swallowing; difficulty in articulation (not aphasic in the early stages of the case); coughing, apparently due to paralysis of the larynx ("crumbs getting down the wrong way").

The well-marked mental symptoms, the development, in the later stages of the case, of motor aphasia and of right hemiplegia showed, however, the true position of the lesion.

Case 6 (Case 35 in the Table.) *Large glio-sarcomatous tumour of the left frontal lobe, involving and completely destroying the whole of the first and the anterior two-thirds of the second and third left frontal convolutions; the posterior third of the second and third left frontal convolutions were slightly implicated; the motor area was not involved.*

J. M., aged 52, publican, was seen with Dr. MacGibbon on March 22, 1892.

Duration. Was quite well until three months ago; since then has suffered from headache, mental apathy, loss of memory, drowsiness, flushings of the face, &c.

General Symptoms. Headache (very severe, chiefly frontal); no vomiting; no giddiness; no tenderness on skull percussion; drowsiness; semi-comatose condition; incoherence of speech; answers questions in monosyllables; talks nonsense; involuntary micturition and defæcation; double optic neuritis. Pulse 45; temperature 98°.

Speech. Motor aphasia appears to be present, but this point is difficult to determine owing to the drowsy, apathetic conditio of the patient.

Motor Symptoms. None.

Knee-jerks. Not obtained; but I speak with hesitation on this point; the patient was a very big, fat man, lying in bed in a semi-stupid condition, and the knee-jerks were consequently very difficult to examine.

Subsequent Progress. Patient died the day after my visit, in a condition of coma.

Post-mortem Appearances. Great increase of intracranial pressure. Left frontal lobe markedly larger than the right; it contained a large glio-sarcomatous tumour which had destroyed the parts enumerated in the heading (see fig. 6).

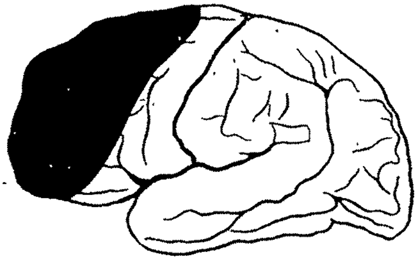

FIG. 6.

Left hemisphere of the brain in the case of J. M. (Case 6), showing the position of the tumour.

Remarks. In this case mental symptoms were very marked; motor aphasia appeared also to be present in the later stages of the case.

(B.)—CASES IN WHICH THE FRONTAL LOBE WAS INVOLVED ALONG WITH OTHER PARTS.

Case 7. (Case 6 in the Table). *Large sarcoma springing from the dura, causing extensive atrophy and destruction of the right ascending frontal and ascending parietal convolutions, the inferior and middle frontal convolutions, the outer half of the island of Reil and the anterior end of the temporo-sphenoidal lobe. No paralysis.*

M. D., aged 20, single, shop-girl, admitted to the Newcastle-on-Tyne Infirmary on January 5, 1877, complaining of headache, vomiting and giddiness. These symptoms thought to be due to "biliousness."

Previous History. Eleven years ago, received a head injury. For the past three years has suffered from headache. Eight months ago, the headache became more severe and the patient began to vomit. Two months ago, she had to give up her situation on account of these symptoms. She has more than once tumbled off her chair, she thinks because of giddiness.

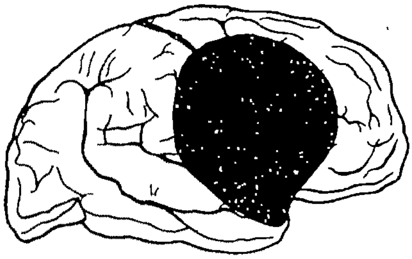

FIG. 7.

Right hemisphere of the brain in the case of M. D. (Case 7), showing the position of the lesion.

General Symptoms. Headache very severe; worst at night, frontal and vertical; vomiting frequent; giddiness frequent; double optic neuritis, very marked in degree.

Mental Symptoms. None except that the patient is much quieter than she used to be.

Speech. No defect.

Motor Symptoms. Absolutely none.

Knee-jerks. Not examined.

Subsequent Progress. Improved under large doses of iodide of potassium.

On *February* 6, 1877, died in an epileptic fit.

Post-mortem Appearances. Bone over the right motor area distinctly thin. The dura mater adherent on the right side over the inferior frontal and inferior parietal areas. Great increase of the intracranial pressure; the convolutions of both hemispheres were much flattened and the sulci effaced. A large sarcomatous tumour, which measured from before backwards 3 inches, from above downwards 3 inches, and from without inwards 1½ inches, sprang from the dura on the right side and

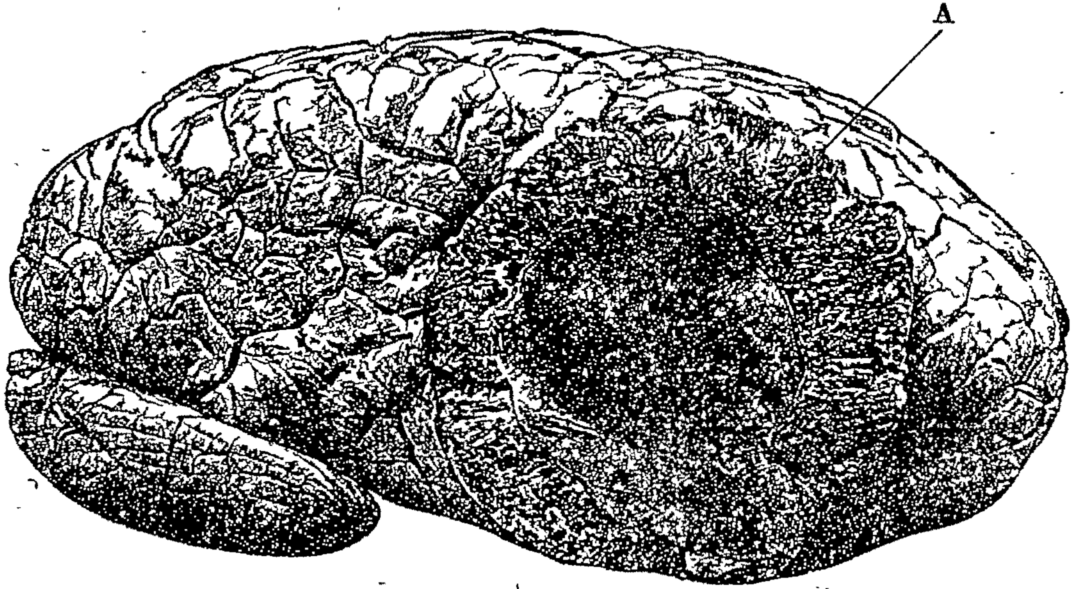

FIG. 8.

The outer surface of the right hemisphere of the brain in the case of M. D. (Case 7), showing the tumour *in situ*. (Copied from a photograph and somewhat reduced in size.)

The letter *A* points to the outer surface of the dura over the centre of the tumour.

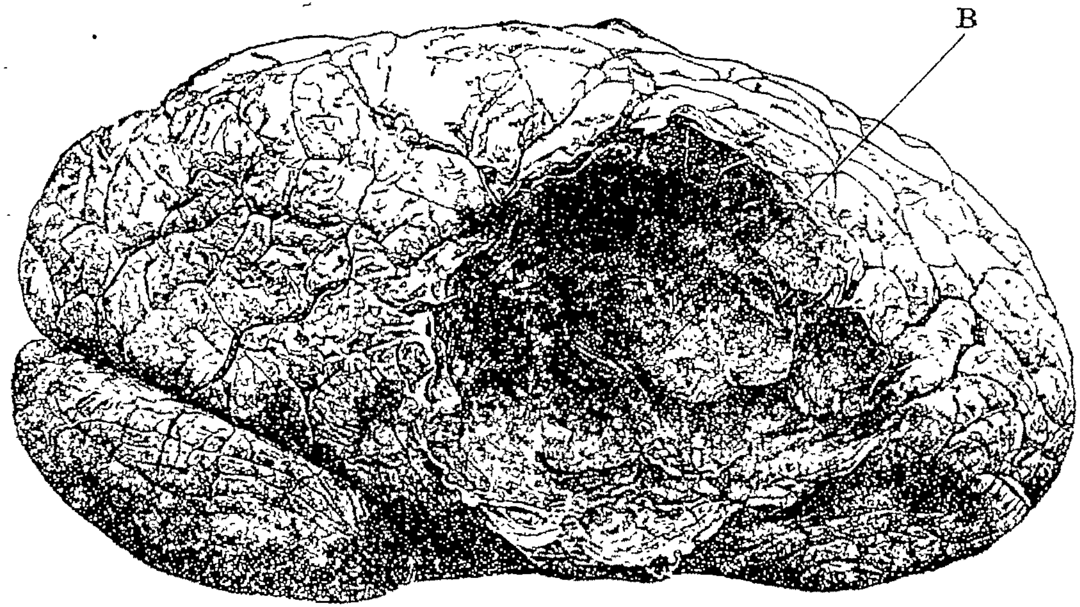

FIG. 9.

The outer surface of the right hemisphere of the brain in the case of M. D. (Case 7), showing the brain after the tumour was removed. (Copied from a photograph and somewhat reduced in size.)

The letter *B* points to the extensive depression on the surface of the brain into which the tumour fitted.

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had destroyed the areas of the cortex enumerated in the heading (see figs. 7, 8, 9 and 10).

The brain and tumour were exhibited in the Pathological Museum of the Edinburgh Meeting, 1898.

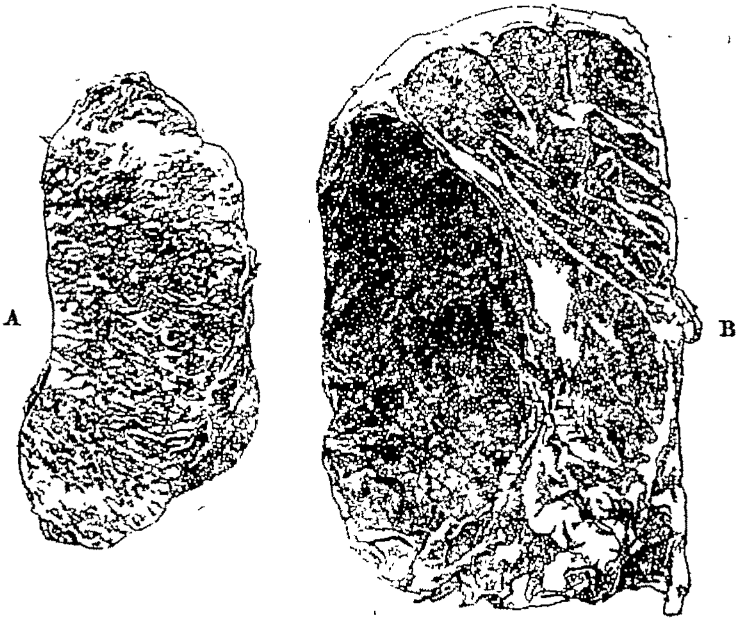

FIG 10.

Transverse vertical section through the right hemisphere of the brain, in the case of M. D. (Case 7), showing the tumour after section, and the depression in the brain tissues produced by it. (Copied from a photograph and somewhat reduced in size.)

The letter *A* points to the tumour.

The letter *B* is placed on the inner (left) side of the right hemisphere, which has been separated from the opposite (left) hemisphere by a section from before backwards in the middle line.

Remarks. In this case a very large portion of the right motor area (ascending frontal and parietal convolutions) of the adjacent (2nd and 3rd right) frontal convolutions and the anterior end of the right island of Reil were completely destroyed, and yet there were no localising symptoms—absolutely no paralysis.

Case 8. (Case 7 in the Table). *Six tubercular tumours of considerable size in different parts of the cerebral hemisphere :* (1) *which measured* ¾ *in. by* ½ *in., situated in the first left frontal convolution ;* (2) *which measured* ¾ *in. by* ½ *in., in the tip of the left occipital lobe ;* (3) *which measured* 1½ *ins. in diameter, in the head of the left corpus striatum ;* (4) *which measured* ⅝ *in. by* ⅝ *in., in the right angular gyrus ;* (5) *which measured* 1¼ *ins. by* ⅜ *in., in the left gyrus fornicatus ;* (6) *which was rather larger than the preceding, situated in the right gyrus fornicatus.*

J. W., aged 5, admitted to the Newcastle-on-Tyne Infirmary on February 27, 1877, suffering from headache and vomiting.

Previous History. Patient received a severe injury to his head two years ago. For the past three months has suffered from headache and vomiting.

General Symptoms. Headache (very severe, frontal, usually worse at night); vomiting; double optic neuritis very marked; voracious appetite.

Localising Symptoms. Impairment of sensibility to touch and pain over the greater part of the body. The left wrist-joint, which is in a state of tubercular disease, is not painful even when pressed and moved.

Mental Symptoms. None observed at the time of the patient's admission to hospital; he was a sharp, intelligent boy. Later, he became dull, stupid and then drowsy.

Motor Symptoms. No paralysis except internal strabismus of the left eye.

Knee-jerks not examined.

Subsequent Progress. On July 5, the patient had a series of general epileptiform convulsions in which the left side of the body was chiefly affected. During his stay in hospital, optic atrophy with blindness developed. He became stupid and drowsy.

On *August* 21, 1877, seven months after admission to hospital, he died.

Post-mortem Appearances. Scalp, bones and membranes were natural. Convolutions were much flattened and the sulci effaced. The brain weighed 2 lbs. 14½ ozs. On cutting into the cerebral substance, tubercular nodules were found in the situations enumerated in the heading. A large, dry, caseous mass was present in the lower lobe of the left lung. Some recent grey tubercles throughout the left lung and in the apex of the right lung. The left wrist-joint was in a state of tubercular degeneration.

Remarks. In this case, six tubercular tumours of considerable size were situated in different parts of the cerebrum (*see* heading), and, except that sensibility to touch and pain were markedly impaired (probably as the result of destruction of parts of both gyri fornicati), no definite localising symptoms were observed.

Case 9. (Case 19 in the Table). *Large glioma and cyst in the left hemisphere, causing complete destruction of the greater part of the left ascending frontal and ascending parietal convolutions and the subjacent white matter, the posterior end of the third left frontal convolution and the greater part of the white matter of the left frontal lobe. No motor paralysis till four days before death. No aphasia.*

M. R., aged 29, female, single, right-handed, admitted to the Edinburgh Royal Infirmary on February 6, 1897, suffering from symptoms suggestive of hysteria or a cerebral tumour.

Previous History. As a girl, the patient suffered from attacks of *petit mal. Two years ago,* after the sudden death of her mother, she began to suffer from fits, some of which were hysterical and others epileptiform in character. The epileptiform attacks commenced with a tingling in the right hand and right leg. *Eight weeks before admission,* the patient had an attack of influenza, and since this attack has been confined to bed for the greater part of the day. *Three weeks before admission,* she, for the first time, complained of headache; it was very severe and referred to the left side of the head and face; of vomiting and dimness of vision. She was nervous and distinctly hysterical. *Four days before admission to hospital,* she complained of slight weakness in the right hand, but no definite loss of power was noticed until two days before admission. On the day of her admission to hospital it was noticed that there was slight dragging of the right leg.

For the past month, the patient has been in a peculiar mental condition, and was thought both by her friends and medical attendant to be hysterical.

Condition on Admission. Patient was in a stupid, dazed, and apparently hysterical condition. There was slight weakness of the right orbicularis palpebrarum, but no other obvious paralysis. She frequently put her right hand up to her head. She resisted vigorously with the right as well as with the left arm while the optic discs were being examined with the ophthalmoscope. She spoke very little and chiefly in monosyllables. Double optic neuritis was marked.

Speech. No speech defect except feebleness of articulation had been noticed before her admission to the hospital.

Knee-jerks, plantar and conjunctival reflexes were normal and equal on the two sides.

Diagnosis. An intracranial tumour; situated in the left hemisphere; nature probably gliomatous.

There were no localising symptoms except the facts :—That the headache before admission had been left-sided; that two days before admission to hospital there had been slight weakness of the right arm; that on the day of her admission to hospital there had been slight dragging of the left leg; and that as the result of my examination slight weakness of the right orbicularis palpebrarum muscle was found to be present. I could not satisfy myself that there was any paralysis of the arms or legs.

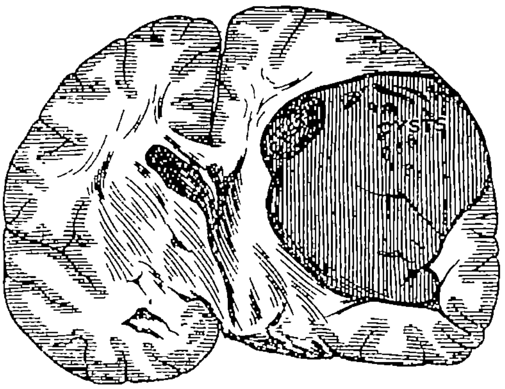

FIG. 11.

Transverse vertical section through the brain in the case of M. R. (Case 9), showing the position and extent of the tumour.
The extent of the tumour is shown by a black line.

Subsequent Progress. The patient died in a convulsion the night after her admission to hospital.

Post-mortem Appearances.—Scalp, skull-cap and membranes normal. Convolutions greatly flattened and sulci effaced, especially over the left hemisphere. The left parietal and frontal lobes considerably larger than the right. A large gliomatous tumour, in which there were several cysts, had infiltrated and destroyed the lower half of the left ascending frontal and parietal convolutions and the white matter passing down from these convolutions to the internal capsule; the posterior end of the second and third left frontal convolutions and their subjacent white matter; the left island of Reil and the left external capsule (see fig. 11). The lenticular nucleus was infiltrated and displaced downwards and inwards, its grey outline being still recognisable. The grey matter of the left third frontal convolution was not completely destroyed, but the white matter immediately subjacent to it was completely infiltrated and destroyed. The upper half of the motor cortex was not directly affected, but the conducting fibres passing from the leg and upper arm centres to the internal capsule were markedly compressed and displaced inwards, *i.e.*, to the right.

The other parts of the brain were absolutely normal. Sections of the brain, showing the tumour, were exhibited in the Pathological Museum of the British Medical Association at the Edinburgh Meeting, 1898.

Remarks. In this case, in which a very large gliomatous tumour with cystic formation had invaded and completely destroyed the lower half of the left ascending frontal and ascending parietal convolutions and the subjacent white matter, there was practically speaking no paralysis. The greater part of the posterior end of the third left frontal convolution and the whole of its subjacent white matter were infiltrated and destroyed, and yet there was no motor aphasia. The patient was right-handed.

TEMPORO-SPHENOIDAL LOBE.

In the next two cases (10 and 11) the tumour involved the temporo-sphenoidal lobe as well as the frontal lobe. In Case 10, the tumour, which apparently had commenced in the left temporo-sphenoidal lobe, had ultimately extended to the left frontal and left occipital lobes. In Case 11, two separate tumours were present—one in the right temporo-sphenoidal and the other in the left frontal lobe.

The first case (Case 10) is of great importance, because the first and second left temporo-sphenoidal convolutions were completely cut off by destruction of their subjacent white matter from the other parts of the brain, and the third left frontal convolution and its subjacent white matter were entirely destroyed; and yet there was no word-deafness and no motor-vocal aphasia.

I may here state that in another case of tumour which I examined *post mortem* some years ago, but which was not under my own care during life, a large glio-sarcomatous tumour had entirely destroyed the posterior half of the first and second left temporo-sphenoidal convolutions, in a right-handed person, without the production of word-deafness. That patient, who was right-handed, suffered from symptoms which were suggestive of hysteria.

The notes of Cases 10 and 11 are as follows:—

Case 10. (Case 22 in the Table). *Enormous gliomatous tumour involving and destroying the greater part of the left frontal and temporo-sphenoidal lobes, and a large part of the left occipital lobe. No aphasia.*

W. S., aged 32, labourer, was sent to me by Dr. Sym as an out-patient at the Edinburgh Royal Infirmary on December 3, 1896, suffering from double optic neuritis and partial right-sided homonymous hemianopsia.

Previous History. The patient, *who is a right-handed man*, was quite healthy till *two-and-a-half years ago.* He then had an epileptic fit. The epileptic fits have continued on an average once a month since; they are general and are not preceded by an aura or any definite localised commencement. *For the past two-and-half years*, the patient has at times complained of slight headache. *Three months ago*, he fell down in the street, apparently as the result of a fit; he remained insensible for thirteen hours after this attack, and has not worked since. On recovering from this attack he complained of dimness of vision in the left eye and pain over the right eye. Since this attack he has been duller and quieter than he was before; his memory has become impaired and he has been absent-minded. He has frequently complained of giddiness.

Condition on Examination. Marked double optic neuritis; partial right-sided homonymous hemianopsia; slight impairment of the power of convergence.

Speech Functions absolutely normal; no word-deafness, no word-blindness.

Motor Functions. No paralysis except the defective convergence mentioned above. *Knee-jerk* slightly more marked on the right than on the left side.

Diagnosis. An intra-cranial tumour; situation left hemisphere, probably far back in the region of the occipital lobe. The only localising symptoms were partial right-sided homonymous hemianopsia, the slight impairment of the power of convergence, the defective contraction of the pupils on convergence, and the slight increase of the knee-jerk on the right side.

Subsequent progress of the Case. December 30, 1896. The patient is duller mentally. The dimness of vision is more marked. The hemianopsia appears to be *in statu quo.* There is slight paralysis of the right external and left internal recti muscles, and defective convergence of the left eye.

During the next three months, the patient continud to suffer from frontal headache and occasional epileptiform attacks. His mental condition became worse, his memory more impaired. He became duller and more stupid. On several occasions he failed to recognise friends in the street (psychical blindness). His sight became more impaired.

In June 1897, the headache was more severe, frontal. The mental dulness and stupidity were much increased. Sight was worse. The gait was distinctly staggering.

On June 20, 1897, he was admitted into the Edinburgh Royal Infirmary. He was very dull and stupid. Could give little or no information about himself. *Hearing* appeared to be slightly defective in both ears. *Speech*: There was no word-deafness and no motor-vocal aphasia. When asked how old he was, where he was born, what his occupation was, where he lived and where he was at the present time, he was unable to answer correctly; but he answered ordinary questions, which did not involve any effort of memory, at once and quite well; he seemed to have no loss of words. The most careful enquiry failed to elicit any evidence of word-deafness or of motor vocal aphasia. There were, in fact, no aphasic defects (word-blindness, word-deafness, or motor-vocal aphasia) during the whole course of the case. *Sight* was *nil* in the left eye and very slight in the right; consequently, at this stage his power of reading and writing could not be tested. Inability to write appeared chiefly to be due to loss of vision, partly perhaps to the weakness and incoordination of the right hand which were present, and partly to the fact that he could not concentrate his attention and make the mental effort required. *Smell* seemed to be normal in both nostrils. *Sensibility* to touch, pain, heat and cold normal, except that there was slight difficulty in localising tactile impressions correctly over both legs.

Motor Functions. Distinct loss of power in the right side of the face, in the right arm and in the right leg. Grasping power as measured by the dynamometer—right, 70; left, 105.

Reflex Functions. Right knee-jerk increased, left diminished. Cremasteric reflex very active on the left, absent on the right side. Fæces passed in bed, apparently as the result of the mental dulness; has some control over the bladder.

September 5, 1897. Right-sided hemiplegia more marked, Mentally duller. Otherwise *in statu quo.*

It was decided to trephine over the left frontal lobe with the object of relieving the increased intra-cranial pressure. The profound mental symptoms suggested that the tumour involved the frontal lobe; but the partial right-sided homonymous hemianopsia which was present at the commencement of the case was suggestive, as has already been stated, of a lesion in the left occipital lobe. The right-sided hemiplegia showed that the motor area or conducting motor tracts in the left hemisphere were implicated. It was obvious, therefore, if the frontal lobe was involved, either that the tumour was of very great size or that there was more than one tumour.

September 9. Mr. Stiles trephined over the left frontal lobe. Scalp, skull cap and membranes were normal. The intra-cranial pressure was enormously increased. No tumour was found. (*Post-mortem* examination showed that the tumour involved the frontal lobe just below the trephine opening.) The patient recovered satisfactorily from the immediate effects of the operation; a cerebral hernia, however, formed at the seat of the trephine wound. The patient's mental condition did not improve after the operation, but he was able to move his right leg a little better than he could before the operation. A few days after the operation a large quantity of cerebro-spinal fluid soaked through the dressings, and large quantities continued to soak through until the date of the patient's *death, October* 8, 1897. After the operation the patient became very thin and took little food.

Post-mortem Appearances. Trephine wound over the upper part of the left frontal lobe. Hernia cerebri surrounded by localised meningo-encephalitis. Great increase of the intra-cranial pressure. Convolutions flattened, sulci effaced. Left hemisphere of the brain much larger than the right and occupied by an enormous gliomatous tumour, which involved the left frontal, temporo-sphenoidal and occipital lobes. The tumour extended from within a quarter of an inch of the tip of the left frontal lobe right back to a point one inch in front of the tip of the left occipital lobe. The second and third left frontal convolutions and their subjacent white matter were entirely destroyed. The whole of the white matter of the left temporo-sphenoidal lobe was entirely destroyed. The grey matter of the left temporo-sphenoidal lobe was almost entirely, but not completely, destroyed; the connections of the grey matter of the first and second left temporo-sphenoidal convolutions were entirely cut off by the tumour in the substance of the lobe (see figs. 12 and 13). A large part of the white matter of the anterior two-thirds of the left occipital lobe was completely destroyed by the new growth.

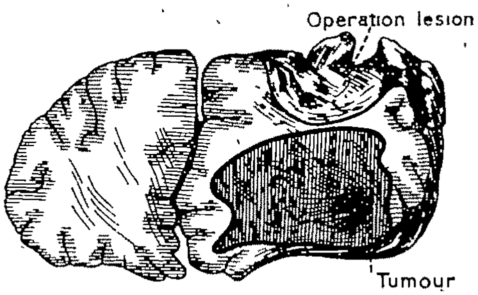

FIG. 12.

Transverse vertical section through the frontal lobes of the brain in the case of W. S. (Case 10), showing the position of the tumour and of the lesion (cerebritis) which resulted from the operation of trephining.

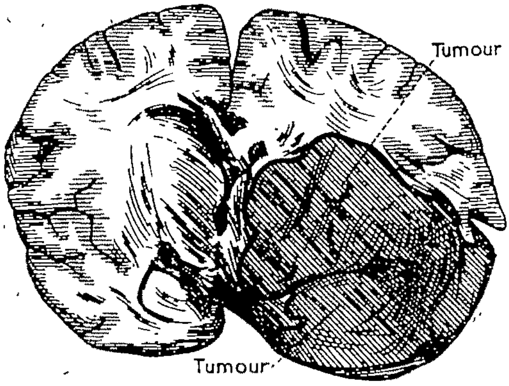

FIG. 13.

Transverse vertical section through the middle of the brain in the case of W. S. (Case 10), showing the extent of the tumour in the temporo-sphenoidal lobe.

The limits of the tumour are represented by a black line.

The parts specified above were not merely infiltrated with gliomatous tissue, but were entirely disorganised and destroyed.

Sections of the brain were exhibited in the Pathological Museum of the Edinburgh Meeting of the British Medical Association, 1898.

Remarks.—In this case, in which the third left frontal convolution and its subjacent white matter were completely infiltrated and destroyed, and in which the greater part of the grey matter of the first and second left temporo-sphenoidal convolutions and the whole of their subjacent white matter were completely infiltrated and destroyed by the new growth, there was no motor-vocal aphasia and no word-deafness.

The extensive destruction of the left temporo-sphenoidal lobe was attended with no localising symptoms, unless the deafness (partial and bilateral) was—and this seems probable—due to this cause.

The loss of memory and the mental impairment were very marked, and suggested a lesion of the frontal lobe.

The partial hemianopsia and the psychical blindness suggested a lesion of the occipital lobe.

Case 11. (Case 37 in the Table). *Glio-sarcomatous cyst in right temporo-sphenoidal lobe, and a gliomatous tumour, with recent hæmorrhage, the size of a large walnut in the posterior end of the second left frontal convolution.*

X. Y., aged 63, excise officer, seen December 23, 1893, complaining of headache, giddiness and dimness of vision.

Previous History. Six months ago the patient was suddenly seized with a sharp pain, as if he had been struck with a stone, behind the right ear. He was quite well previously. He has, at times, suffered from the same pain since; and the headache, giddiness and dimness of vision have since developed.

General Symptoms. Headache (intense, right-sided, deep and internal); also shooting, superficial, neuralgic pains referred to the right side of the head and the lobe of the right ear; no vomiting; giddiness very marked; dimness of vision marked (is unable to read any test types at 18 feet). Double optic neuritis very marked.

Mental Symptoms. Absolutely none.

Speech Symptoms. None.

Motor Symptoms. None.

Knee-jerks equal and normal on the two sides.

Diagnosis. An intracranial tumour, probably in some part of the right hemisphere (because of the locality of the pain). Absolutely no other localising symptoms.

Subsequent progress of the Case. March 20, 1894. Rather better. Neuralgic pain less. Complains of pain, numbness and coldness behind the right ear and down the right side of the neck. Optic neuritis distinctly less; sight somewhat clearer.

In April, 1895, spat up a considerable quantity of bright fluid blood.

May 28, 1895. Gave a somewhat exaggerated statement of the amount of blood which he had spat up. Is in a restless mental condition. Sight greatly improved; says that he is "able to play a fair game at golf." For the past year, has had little or no headache or giddiness. Still complains of a numb, cold feeling behind the right ear. The optic neuritis has quite disappeared, leaving slight neuritic atrophy; his sight is dim, but he has no difficulty in reading and writing (tested by myself).

In April and May, 1896, had three epileptiform attacks.

June 18, 1896. Had another severe fit yesterday. The onset of the attack was preceded by an aura of jargon-reading (he was reading aloud to his daughter at the time and suddenly commenced to read a lot of nonsense and jargon which she could not understand), and by dimness of vision; he lost consciousness; there were no spasms. The attack was followed by complete temporary motor aphasia, word-blindness and agraphia.

On examination, June 18, 1896, I found the patient in a dazed and confused mental condition. He knew Dr. Menzies, but did not know me. There was no word-deafness. There was slight motor aphasia (he used some wrong words); but he answered most questions which were put to him quite correctly. There was distinct word-blindness and some agraphia. He could not read *his own name*; could not read the letter *a*. When asked to write his name, wrote his Christian name correctly and his surname incorrectly, and then read what he had written as his own name. Could not read his name (when written correctly) a few minutes afterwards. There did not appear to be any hemianopsia, but owing to the confused mental condition of the patient it was difficult to determine this point with certainty. There was no paralysis. The knee-jerks were equal and normal.

On August 4, had another fit.

For some weeks after this attack, the patient improved.

On August 29, was very well; took a drive and walked two miles of the way home.

After this date, he got worse; suffered from headache and fearful giddiness. While in bed during the first half of September, he wrote a few short business communications and read the newspaper. After this date, he did not write at all, was unable to sign his own name (to draw a cheque). His doctor thought that the inability to write was due to dimness of vision, but this is perhaps doubtful. Did not read. At times he became very excited ("pranced round the room in his nightshirt," &c.); at times was mentally bright, at other times seemed almost in a condition of dementia. There was never any motor paralysis; he could hold a pen quite well.

Two days before death he became rapidly worse (semi-comatose); and it was apparently at this date that the recent hæmorrhage, described above, occurred.

He died on *October* 22, 1896.

Post-mortem Appearances. Scalp, skull-cap and dura were normal. There was no meningitis. The vessels were healthy. The convolutions on both sides of the brain, but especially on the left side, were moderately flattened and the sulci to some extent effaced. The middle part of the second right temporo-sphenoidal convolution had a yellowish appearance, as seen from the outside, as if from internal softening. In the right temporo-sphenoidal lobe there was a slit-like cavity (cyst) measuring two inches in length by half an inch in breadth at the thickest part. This cavity was surrounded by condensed brain tissue, which on microscopical examination was found to be gliomatous in character.

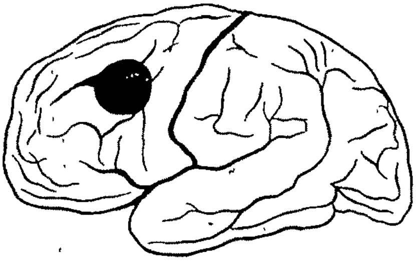

FIG. 14.

Left hemisphere of the brain in the case of X. Y. (Case 11), showing the position of the tumour.

A recent hæmorrhagic extravasation the size of a large walnut was situated in the posterior end of the second left frontal convolution. On microscopical examination, the hæmorrhage was found to be poured out from the vessels of a gliomatous tumour. The tumour and hæmorrhage were sharply localised to the posterior end of the left frontal convolution (see fig. 14). The third left frontal convolution and the subjacent part of the motor area (left ascending parietal convolution) were not implicated. There was no lesion of the left angular gyrus or supramarginal convolutions. The other parts of the brain were healthy.

The lungs and heart were healthy. No intrathoracic cause for the hæmoptysis was found.

Remarks.—There is every reason, I think, to suppose that in this case the lesion (gliomatous tumour and cyst) in the right temporo-sphenoidal lobe was the first to develop, and that the tumour in the second left frontal convolution was only developed in the later stages of the case. Until shortly before the patient's death, there were absolutely no localising symptoms (unless the pain in the right side of the head and the numbness and coldness behind the right ear were due to the tumour in the right temporo-sphenoidal lobe). The general symptoms of an intracranial tumour (headache, giddiness and double optic neuritis) were, however, marked from the first.

In the later stages of the case, more definite localising symptoms were developed, viz., epileptiform attacks, one of which commenced with jargon-reading and was followed by temporary motor-vocal aphasia, word-blindness and agraphia. During the last six weeks of his life the patient was unable to read and to write; his medical attendant thought this inability was due to loss of vision, but the correctness of this opinion is, perhaps, doubtful. The agraphia was certainly not due to motor paralysis; the patient could hold a pen quite well. The question, of course, arises whether the agraphia was not directly due to the very localised lesion (tumour) in the posterior end of the second left frontal convolution (Exner's writing-speech centre), and whether the word-blindness was not indirectly due to the same lesion. It is, of course, impossible to answer the question, either one way or the other, with certainty; but the possibility of the agraphia and word-blindness being due to this cause (destruction of Exner's writing-speech centre) must be entertained; and in this connection it must be remembered that in Case 4, in which the posterior end of the second left frontal convolution was completely destroyed by a tumour, and in which there was no agraphia, the destruction was very slow and chronic. Personally, I see no reason to believe in the existence of a special writing-speech centre, but I record the present case, which may perhaps be advanced in support of Exner's view, impartially and with an open mind.

SUMMARY OF THE LOCALISING SYMPTOMS (IN THE CASES WHICH HAVE BEEN RELATED) SUGGESTIVE OF A TUMOUR IN THE FRONTAL LOBE.

In seven of the eleven cases in which the frontal lobe was involved (viz., in Cases 1, 2, 5, 6, 9, 10, and 11), well marked mental symptoms were present; in the remaining four cases (viz., 3, 4, 7 and 8), there were no definite mental symptoms. Nevertheless, I am strongly of opinion that tumours localised in the frontal lobe are more apt to be attended with well marked mental symptoms (mental enfeeblement, loss of memory, loss of the power of attention, change in disposition, irritability, taciturnity, obstinacy, incoherence and rambling of speech, delusions of suspicion, &c.) than localised tumours in any other part of the cerebral hemispheres.

In Cases 1 and 2, in which the tumour involved identical parts of the frontal lobe (in Case 1 the right and in Case 2 the left frontal lobe being the seat of the tumour), the mental symptoms were practically the same, viz., a marked change in disposition and temper; at times, both patients were irritable and obstinate, at other times, sullen, stupid and depressed; in both cases, memory was markedly impaired; and in both cases there was grinding of the teeth during sleep.

In one Case (5) a marked tendency of the head to fall to the opposite side was noted.

Tumours in the posterior end of the frontal lobe frequently (by pressure on, or implication of, the motor fibres passing from the motor cortex to the internal capsule) produce loss of power on the opposite side of the body (Cases 1, 2, 3, 5,); the loss of power sometimes affects both legs, and in some cases the loss of power frequently recurs as a temporary condition—sudden giving way of the leg or legs (Case 1).

Tumours on the surface of the posterior end of the frontal lobe may, by irritation of the adjacent motor cortex, produce Jacksonian epilepsy (Case 3).

Tumours in the posterior end of the left frontal lobe, which involve the motor-speech centre, may produce motor-vocal aphasia (Cases 5 and 7), but the motor-vocal speech centre or its subjacent white matter may be entirely destroyed by a tumour without any motor aphasia (Cases 9 and 10).

In Case 4, complete but slow destruction of the posterior end of the second left frontal convolution was not attended with any agraphia; in Case 11, destruction of the posterior end of the second left frontal convolution was (perhaps) attended with agraphia and some word-blindness.

A voracious appetite was present in one case (8).

The *general symptoms* which result from tumours of the frontal lobe are in no way peculiar.

In the 11 cases detailed above *headache* was present in 10 (and not noted in 1 case); in 7 of the 10 cases the headache was very severe. In 3 cases the headache was frontal; in 2 cases, frontal and vertical; in 1 case, frontal and occipital; in 1 case, frontal and parietal; in 1 case, frontal and temporal; in 1 case, referred to the right side of the head and face (the side of the tumour); and in 2 cases the locality of the headache is not noted.

Vomiting is perhaps less frequent and I think usually less severe than in tumours situated further back. In the 11 cases recorded above, vomiting was present in 6 (marked in 5, slight in 1) and absent in 5 cases.

Giddiness was present in 6 cases (marked in 5, slight in 1); absent in 2 cases, and not noted in 2 cases.

Optic neuritis was present in 9 cases (marked in 7, slight or moderate in 2); in one case the optic neuritis was much more marked in one eye (that on the side of the tumour); absent in 1 case and not noted in 1 case.

General epileptiform convulsions occurred in 6 cases; and localised spasms (Jacksonian epilepsy) in 2 cases; in the remaining 3 cases there were no spasms or convulsions.

Condition of the knee-jerks. In 5 of the 11 cases the condition of the knee-jerks was not noted (these cases all occurred more than twenty years ago); in 3 cases the knee-jerks were equal and normal on the two sides; in 1 case, in which the tumour was situated in the left frontal lobe (Case 5), the knee-jerk was feeble on the right, and active on the left side; in 1 case, in which the tumour involved the left frontal, temporo-sphenoidal and occipital lobes (Case 10), the knee-jerk was increased on the right and diminished on the left side.

SUMMARY OF THE LOCALISING SYMPTOMS (IN THE CASES WHICH HAVE BEEN RELATED) DUE TO A TUMOUR IN THE TEMPORO-SPHENOIDAL LOBE.

In both of the cases (10 and 11) in which the tumour involved the temporo-sphenoidal lobe there were, practically speaking, no localising symptoms; and I have been in the habit of regarding the temporo-sphenoidal lobe as *par excellence the* silent area of the brain. So far as my experience enables me to judge, localising symptoms are most certainly and obviously produced in those cases of intra-cranial tumour in which the tumour is situated at the base of the brain, and in which the cranial nerves at their point of origin from the nervous tissues are directly involved by the new growth. Then, in the relative order with which they can be most easily and certainly diagnosed (*i.e.*, in which the localising symptoms are most certain and constant), I would place tumours in the following situations:—(2) pons Varolii and medulla oblongata; (3) centrum ovale (cases in which the fibres of the internal capsule or the optic radiations of Gratiolet are directly implicated)

(4) tumours of the occipital lobe, involving the half-vision centre or the optic radiations of Gratiolet; (5) tumours of the motor area, in which the tumour produces irritation and gives rise to localised epileptiform convulsions; (6) tumours of the cerebellum; (7) tumours of the frontal lobe; (8) tumours of the upper part of the parietal lobe (*i.e.*, tumours which do not involve the angular gyrus or its subjacent white matter); and last of all, the most difficult to diagnose and locate, (9) tumours of the temporo-sphenoidal-lobe, and especially, of course, tumours of the right temporo-sphenoidal lobe.

I need hardly say that this is merely a rough classification. Tumours of the *central* lobe of the cerebellum, for instance, can usually be located and diagnosed with great certainty. The same statement probably also applies to tumours involving the left angular gyrus (in right-handed people).

In Case 10, there was some impairment of hearing in both ears. In Case 11, the patient complained of pain, numbness and coldness behind the right ear (the side of the tumour); this was perhaps a localising symptom. Tumours of the left temporo-sphenoidal lobe may of course give rise to word-deafness, but this symptom was not present in Case 10, in which the left temporo-sphenoidal lobe was, practically speaking, completely destroyed.

ISLAND OF REIL.

In addition to Cases 9 and 10, in which the tumour involved the left island of Reil, I have met with one other case in which the island of Reil (on the right side) was destroyed by a tumour. The notes are as follows:—

Case 12. (Case 18 in the Table). *Two gliomatous tumours*—(1) *involving the left centrum ovale, and* (2) *the right island of Reil, lenticular nucleus and adjacent parts.*

M. P., aged 63, female, nurse, a right-handed woman, admitted to the Edinburgh Royal Infirmary on September 25, 1896, suffering from loss of power in the right arm and leg, numbness in the right side of the body, headache, giddiness and occasional dimness of vision.

Previous History. Has suffered from headache for five weeks. Numbness and loss of power in the right arm commenced three weeks ago; it first affected the shoulder and gradually extended down the arm; and then affected the leg.

General Symptoms. Headache; occasional giddiness; optic neuritis present (verified on *post-mortem* examination).

Motor Symptoms. Complete loss of power in the right arm, partial loss of power in the right leg. No paralysis of the right side of the face.

Knee-jerks both exaggerated.

Sensibility. Some impairment of tactile sensibility on the right side of the body (arm and leg). Sight good. No hemianopsia.

Speech. The articulation a little thick, but no aphasic defect.

On *September* 28, 1896, patient took what she termed "a funny turn," shivered but did not feel cold; there was no rise in temperature; she felt in a nervous peculiar state. During the attack, twitchings were observed in the upper part of the right arm, the right side of the chest and the right side of the abdomen. There was no loss of consciousness. The nurse said that she had difficulty in speaking during the seizure. The attack was not followed by any increase of the paralysis. Sight was dim for two hours after the attack. At 8 *p.m.*, she complained of severe headache, frontal, affecting both sides. At 9.30 *p.m.*, she vomited and there was distinct difficulty of articulation and in expressing herself. At 11 *p.m.*, she was stupid and seemed to have difficulty in understanding what was said to her, and in answering questions, but there was no defect of articulation.

October 12, 1896. Did not answer the House-Physician at his evening visit.

October 13, 1896. Has a distressed look; cannot be got to answer any questions; complete motor aphasia; appears to understand everything that is said to her and makes signs intelligently in answer to the questions which are put to her, but does not speak. The *left* side of the face is paralysed.

October 16, 1896. The paralysis of the left side of the face is more marked. Temperature 101°.

October 18, 1896. Looks rather better. Answered some questions to-day intelligently, but for the most part in monosyllables. In answer to the remark, "Glad you are better," answered, "Yes"; in answer to the question, "Have you any pain?" answered, "No"; in answer to the question "Is your arm feeling any stronger?" answered "A little better."

October 19, 1896. The left side of the body became rigid, and the patient passed into a condition of coma. Both arms appear to be paralysed. Eyeballs while at rest turned to the right; nystagmoid jerkings of the eyeballs to the left, with slow return to the middle line, were present; pupils equal and dilated; they react to light; conjunctival reflex present. Pulse and respirations both very rapid. Some difficulty in swallowing.

October 23, 1896. Patient died. The temperature ran up to a high point just before death. For eighteen hours before death, the respirations numbered 70 per minute.

Post-mortem Appearances. Scalp, skull-cap and membranes flattened and sulci effaced. Weight of the brain = 3 lbs. 4 ozs. Arteries at the base normal. On cutting up the brain, a gliosarcomatous tumour, measuring 1¾ in. by 1 in. in breadth, was present in the white matter of the left centrum ovale, just in front of the left angular gyrus.

In the right hemisphere, a recent hæmorrhage which subsequent microscopic examination showed had been poured out from the vessels of a gliomatous tumour, had almost completely destroyed the lenticular nucleus and the anterior part of the right internal capsule. In front of the hæmorrhage a mass of gliomatous tissue involved the caudate nucleus and the greater part of the island of Reil and its subjacent white matter. There were numerous small hæmorrhages in the gliomatous tissue which infiltrated the island of Reil.

Remarks. The most important point in this case, so far as the present discussion is concerned, is that a tumour with hæmorrhage in the *right* island of Reil and adjacent parts produced motor aphasia, which would no doubt, if the patient had lived, have been merely temporary. I have met with other cases in which a sudden lesion (hæmorrhage, &c.) in the region of the *right* motor-vocal speech centre has in right-handed persons produced temporary motor-vocal aphasia.

OCCIPITAL LOBE.

In my experience tumours are comparatively rarely met with in the occipital lobe. Two cases only, verified by *post-mortem* examination (in addition to Cases 8 and 10, which have already been detailed), have been under my own observation during life. The notes are as follows:—

Case 13. (Case 11 in the Table). *Sensory (visual) Jacksonian epilepsy, due to the presence of a cicatrix, the result of an old syphilitic gumma on the outer surface of the posterior end of the left occipital lobe.*

W. G., aged 60, usher in a school, formerly a soldier, seen at the Edinburgh Royal Infirmary on March 5, 1887, complaining of frequent flashes of red and white light in the right eye.

Previous History. At the age of 24, the patient had syphilis (a serpiginous scar on the tibia, the result of an old syphilitic ulceration, is still present). The same year (1848) he received a severe head injury. *In* 1863, he complained of severe headache limited to the back and top of the left side of the head; the pain was worse at night; at this time a swelling developed 1½ inches behind and slightly above the left parietal eminence, and he took an epileptic fit. He has had several epileptic fits since; the third and fourth, which occurred during the years 1883 and 1884, were preceded by flashes of light in the right eye. *From* 1877 *up to* 1887, when I first saw the patient, he continued at long intervals to have flashes of light in the right eye. The attacks occurred on an average about once a year; each attack, which consisted of very numerous paroxysms, usually lasted for three or four weeks. The paroxysms occurred every five or ten minutes, and lasted from half a minute to three minutes; they consisted of flashes of light in the right eye; the light was said to be red and white like a magic lantern. For some days after the attack the patient was unable to see to the right side (right-sided homonymous hemianopsia).

Present Condition. When the patient came under my observation he was suffering at frequent intervals from the paroxysms described above. The fields of vision were carefully mapped out with the perimeter (the charts have been published in my "Atlas of Clinical Medicine," plate xxxvi., figs. 3 and 4). They show right-sided homonymous hemianopsia both for white and colours, and some contraction of the sound (seeing) halves of the visual fields. During the paroxysms, the patient complained of a noise like a steam-engine in the left ear. The fundi were quite normal and there was no word-blindness.

Progress of the Case. Under treatment (iodide of potassium) the paroxysms and flashings soon subsided and the hemianopsia almost completely disappeared, the fields for white and green remaining somewhat contracted (see charts, "Atlas of Clinical Medicine," plate xxxvi., figs. 5 and 6). The headache also completely disappeared. The patient was at the time suffering from an epithelioma of the tongue, and operative procedure (which would otherwise have been considered) was contraindicated.

The patient died several months after he first came under my observation.

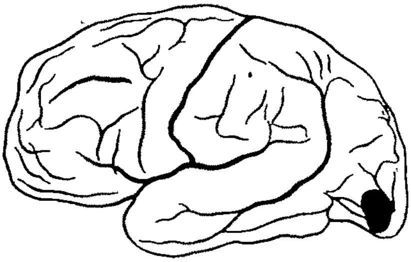

FIG. 15.

Left hemisphere of the brain in the case of W. G. (Case 13), showing the position of the lesion.

Post-mortem Appearances. The membranes were adherent over the outer surface of the anterior part of the left occipital lobe and over the adjacent surface of the cerebellum (see fig. 15, also "Atlas of Clinical Medicine," plate xxxvii., fig. 4). The brain substance was sclerosed and atrophied and had evidently at one time been the seat of inflammatory changes (syphilitic gumma, &c.).

Remarks.—In this case an irritative lesion (cicatrix of an old syphilitic gumma) on the outer surface of the posterior end of the left occipital lobe produced frequently recurring attacks of sensory (visual) Jacksonian epilepsy—flashes of light referred to the right eye—followed by temporary sensory paralysis (*i.e.*, right-sided homonymous hemianopsia).

Case 14. (Case 32 in the Table). *Numerous melanotic sarcomatous tumours in the brain, one situated in the tip of the left occipital lobe, another in the middle lobe of the cerebellum, which was entirely destroyed.*

S. E. M., aged 26, female, single, seen on September 28, 1886.

Previous History. Patient has had a pigmented mole on the right shoulder all her life. After a direct injury (blow with a stick) received about the age of 12 or 13, the pigmented mole enlarged. In 1881, it was the size of a half-crown piece; it was then scraped. In 1885, it had returned and then formed a fungating tumour the size of a walnut. On October 23, 1885, it was excised. The patient remained well until July 26, 1886, when she began to complain of flashes of light in the eyes, intense headache and vomiting.

Condition on September 28, 1886. *General Symptoms.* Headache (intense, especially on the right side); vomiting; giddiness; double optic neuritis.

Localising Symptoms. Patient suffered very frequently (50 or more in the twenty-four hours) from paroxysmal attacks lasting for five minutes at a time, from headache, flushing and flashes of light in the eyes; the light was said to be especially bright in the right eye; it had the brilliancy of an electric light, and varied in size from a button to a large globe. During these paroxysms the patient stated that she was completely blind. After an attack, which I personally witnessed, passed off, there did not appear, so far as could be determined by the rough test, to be any hemianopsia.

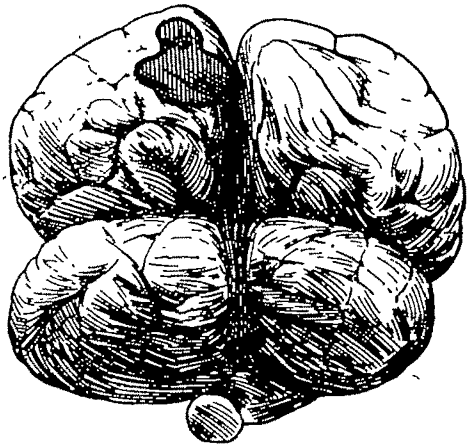

FIG. 16.

Posterior end of the brain in the case of S. E. M. (Case 14), showing the position of the lesion (outlined by a black line).

Mental Faculties. Quite clear. No emotional or hysterical symptoms.

Motor Symptoms. Difficulty in directing the movements of the left arm. *Knee-jerks* active and equal.

Diagnosis. Melanotic sarcoma in the brain; probably several deposits, one involving and irritating the half vision centre in the left hemisphere.

Subsequent Progress. The patient continued to suffer from the same symptoms. During the month of October, 1886, paralysis of the left arm and leg developed.

On *November* 2, 1886, the patient died.

Post-mortem Appearances. A nodule of melanotic sarcoma, the size of a large walnut on the surface of the posterior end of the left occipital lobe just above its tip (see fig. 16). The subjacent white matter was infiltrated, but only partly destroyed. Numerous other melanotic deposits in the brain, the frontal and occipital lobes being chiefly involved. A small nodule in each island of Reil. A nodule of some size in each optic thalamus. A small nodule in the pons involving the motor tract on the right side. A large nodule in the middle lobe of the cerebellum, which was entirely destroyed. Several small nodules in the lateral lobes of the cerebellum.

Remarks.—In this case, irritation of the left half-vision centre produced frequently recurring flashes of light in the eyes, especially in the right (opposite) eye.

In addition to the two cases which have just been related, the occipital lobe was also the seat of a tumour in two of the cases which have been already described (Cases 8 and 10). In Case 10, there was partial right-sided hemianopsia and mind-blindness due to involvement of, either the white matter of the anterior end of the left occipital lobe, below the angular gyrus, or of the parietal lobe.

PARIETAL LOBE.

Only one case with *post-mortem* has come under my observation in which the angular gyrus was involved by a tumour. The notes of that case, in which the right angular gyrus and the adjacent parts were the seat of the lesion, have little value for the present discussion. The case occurred twenty-four years ago. My want of knowledge, at that time, of the localising symptoms due to brain lesions and the defective mental condition of the patient sufficiently account for the comparatively imperfect nature of the clinical record. It is briefly as follows:

Case 15. (Case 1 in the Table). *Syphilitic tumour involving the right angular gyrus and the adjacent parts of the parietal and occipital lobe, with extensive softening of the subjacent white matter.*

R. S., aged 41, chemist, single, admitted to the Newcastle-on-Tyne Infirmary on November 12, 1874, suffering from left-sided hemiplegia, headache, &c.

Previous History. The patient had syphilis many years ago. Has suffered from headache and "rheumatism" for the past year. Three months ago left-sided hemiplegia suddenly developed.

General Symptoms. Headache (marked) mental impairment and loss of memory; left hemiplegia and left hemianæsthesia affecting the arm and leg; dimness of vision; post-neuritic atrophy, and syphilitic choroiditis; tibial nodes. The patient was fat and well nourished.

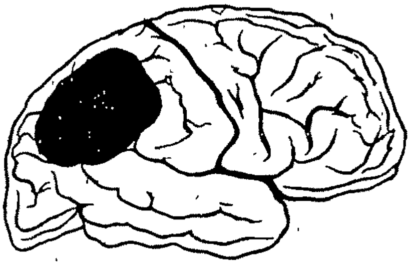

FIG. 17.

Right hemisphere of the brain in the case of R. S. (Case 15), showing the position of the lesion.

Subsequent Progress. The patient continued to suffer from recurring headaches. There was some slight improvement in the hemiplegia and hemianæsthesia.

On December 8, 1874, he had a general epileptic fit which was followed by coma and death.

Post-mortem Appearances. A hard, nodulated, old syphilitic tumour, the size of a walnut, was situated on the outer surface of the right parietal lobe. The dura over the posterior end of the right hemisphere was thickened. The angular gyrus, the upper and middle parietal convolutions, the anterior end of the occipital convolutions and the subjacent white matter of the *right* hemisphere were implicated and more or less extensively destroyed by softening (see fig. 17). Syphilitic cicatrices were present in the liver and nodes on the tibia.

Remarks.—With reference to the occurrence of word-blindness in cases of cerebral tumour, I may again point out that in Case 11 there was distinct but temporary word-blindness, apparently due to the (indirect) irritation produced by a tumour which was sharply limited to the posterior end of the second left frontal convolution.

Case 16. (Case 39 in the Table). *Fibro-cellular tumour involving the left upper parietal convolution, entirely latent, complicated with a large cerebral abscess, acutely developed in the subjacent white matter.*

A. B., aged 40, seen on December 4, 1895.

Previous History. Patient was a strong, healthy man who had never been previously ill. He had not suffered from syphilis or ear disease, and he had never received any head injury. On December 2, 1895, he complained of pain in the left parietal region. On December 3, he experienced a numb feeling in the right hand and some difficulty in writing and using his knife at lunch. Thinking these symptoms were due to biliousness, he took a blue pill before going to bed on the evening of December 3. During the night of December 3 he had three very severe epileptic fits; the convulsions were general and attended with loss of consciousness. After the fits he complained of great pain in the abdomen.

Present Condition. When seen by me on the morning of December 4, the patient was quite sensible and able to give a detailed account of his sensations, &c. The pulse and temperature were normal; there was no paralysis; the knee-jerks were equal and normal; the pupils were equal and active; the optic discs were normal; there was no hemianopsia and no aphasia, either sensory or motor; there was no tenderness on skull percussion; hearing was normal, and there was no ear disease.

The chief complaint was abdominal pain and tenderness, which, after careful consideration, it was decided were the result of the violent spasmodic contractions of the abdominal muscles during the fits. The urine was normal; the heart and arteries were normal. There was no suspicion of alcoholic excess or of any form of intoxication.

On December 9, the abdominal pain and tenderness had disappeared. There had been no return of the convulsions. The temperature had remained subnormal; the pulse rather slow (60 to 65 per minute). Since the last consultation there had been more or less headache, and at times it had been very severe; it was chiefly referred to the left side of the head. For the past two nights the patient had been very restless and anxious about himself, and had complained of a numb feeling in the right arm and leg.

On examination, distinct loss of power in the right side (face, arm, and leg) was found to be present. The loss of power was more marked in the leg than in the arm. There was also some loss of tactile sensibility on the right side of the body, more particularly in the leg. There was no aphasia, no word-deafness, no word-blindness, no motor vocal aphasia, and no hemianopsia. Well-marked double optic neuritis was now present. The pupils were equal and active; temperature normal; pulse 60; tongue clean. The urine still continued free from albumin. The heart and arteries were perfectly normal.

On December 11, the patient, who had had a restless night, was obviously worse, the paralysis much more marked. There was also now some difficulty in speaking, apparently due to motor aphasia. Impairment of tactile sensibility on the right side of the body was also more marked. The optic neuritis was more distinct. The pupils still remained equal, and contracted actively to light. The temperature was 92·2°, and the pulse 64. Since the date of the last consultation two days ago, there have been no convulsive twitchings and no severe headache.

On the afternoon of this day, December 11, Dr. John Duncan met Drs. Russell Wood, Playfair, and myself in consultation. He agreed as to the difficult and exceptional nature of the case, and as to the probability of the lesion being thrombosis rather than tumour. With us he thought that in the absence of any obvious cause, cerebral abscess was a most unlikely condition, and might in all probability be excluded. Under these circumstances it was decided not to advise any operative procedure.

On December 12, the patient was worse; motor aphasia more marked; temperature normal; pulse 60; the condition otherwise unchanged.

At 1.30 a.m. on December 13, the breathing became stertorous, and the patient passed into a condition of coma, the temperature running up in the course of a short time to 102·6°. Death occurred at 4 a.m.

At the post-mortem examination, which was made by Professor Robert Muir, the convolutions of the brain were found to be flattened and effaced, more especially on the left side. At one or two places on the surface of each hemisphere the subarachnoid fluid was slightly turbid, and there were minute particles of lymph in the sulci. The membranes at the base were quite healthy. There were no emboli or thrombi in any of the vessels. The arteries and veins of the brain were absolutely normal.

On examining the surface of the brain, a tumour was found on the left side. Its posterior border was situated at the junction of the parietal and occipital lobes, and its inner border half an inch from the middle line. It was irregularly quadrangular in shape, about three-quarters of an inch in diameter, and extended down into the brain as a blunt wedge for about three-quarters of an inch. The tumour was sharply marked off from the surrounding brain tissue.

On transverse section through the brain, an abscess the size of a large hen's egg was found in the middle of the left hemisphere. It was situated in the centrum ovale, rather nearer the posterior than the anterior end of the brain. At its nearest point to the cortex it was about an inch below the grey matter. The contents of the abscess consisted of a thin and extremely stinking pus. The brain substance forming the wall of the abscess was fairly firm and dense, more especially at one point underlying the tumour.

The dura mater, the venous sinuses, the bones of the skull, the middle and internal ear, the nose, etc., were all carefully examined, and were found to be absolutely normal. The heart, arteries, lungs, liver, spleen, kidneys, and other abdominal and pelvic viscera were quite healthy. The most careful search failed to detect any local source for the abscess, or any disease in any of the organs of the body other than the brain.

(The full notes of the case, with a discussion of the diagnosis and a detailed account of the treatment which was adopted, are published elsewhere.[1])

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[1] *Scottish Medical and Surgical Journal*, Nov., 1897, p. 972.

BASAL GANGLIA.

(a) *Optic Thalamus.*

In one case (Case 13 in the Table), the tumour seemed to have its primary seat in the right optic thalamus, but there were no symptoms to indicate that this was the position of the lesion. The case was perhaps the most deceptive, so far as localising symptoms were concerned, which has come under my notice. The notes are as follows:—

Case 17. (Case 13 in the Table). *Glio-sarcoma of the right optic thalamus; symptoms indicative of a syphilitic gumma involving the right leg centre.*

R. G., aged 50, an old soldier, gatekeeper at Holyrood, was seen at the Edinburgh Royal Infirmary on March 18, 1893, suffering from headache, numbness and stiffness in the left leg, occasional spasmodic twitchings in the left leg beginning in the left big toe.

Previous History. Had syphilis 26 years ago.

General Symptoms. Headache (severe, referred to the right motor area, worse at night); tenderness on pressure and percussion over the right motor area, exactly localised to the leg and upper arm centres; giddiness (occasional); the patient had on more than one occasion tumbled, he thought partly as the result of giddiness and partly in consequence of giving way of the left leg; the discs were ill-defined, the veins in the right fundus being dilated, but there was no definite optic neuritis.

Localising Symptoms. Tenderness over the leg and arm centres on the right side; attacks of Jacksonian epilepsy occurring several times a day, the spasm beginning in the left big toe; exaggeration of the left knee-jerk. There was no swelling or alteration in the scalp at the seat of the pain and tenderness.

Diagnosis. A cortical gumma in the position of the right leg centre.

Treatment. Iodide of potassium, twenty grains three times daily.

Subsequent Progress of the Case. Speedy relief of the headache and disappearance of the spasms. When last seen, the patient said that he was quite well, but some tenderness on percussion could still be elicited over the right motor area. Was advised to continue the iodide.

Some weeks later, the head symptoms returned and were not relieved by the continued administration of the iodide. The patient was therefore sent by his medical attendant (who knew that I had no male beds) into the Infirmary, where he was seen by Dr. Gibson, who, not knowing that I was connected with the case, arrived at the same diagnosis—a cortical gumma in the right-leg centre—and advised, as the iodide had failed to give relief, that the patient should be trephined. This was accordingly done by Mr. Alexis Thomson. No tumour was found. The operation wound healed satisfactorily. The patient died some time afterwards.

Post-mortem Appearances. The scalp, skull-cap and membranes quite normal. Some flattening of the convolutions and obliteration of the sulci, especially on the right side. A glio-sarcomatous tumour about the size of a small egg occupied the position of the right optic thalamus and had slightly encroached upon the motor fibres of the pyramidal tract.

Remarks. In this case, the symptoms were clearly indicative of a syphilitic gumma of the right leg-centre; the tumour was a glioma of the right optic thalamus; it had apparently produced irritation of the leg fibres of the internal capsule.

In addition to this case, in which the optic thalamus was the primary seat of the new growth, the optic thalamus was involved along with other parts in three other cases (10, 13, and 23). In Case 13, which has already been related, melanotic deposits of considerable size were present in each optic thalamus. In Case 23 in the Table, a very large glio-sarcomatous tumour, which had commenced in the right centrum ovale and involved the whole of the internal capsule and the optic radiations of Gratiolet, had extended to the right optic thalamus; but, since tumours of the centrum ovale are not included in this discussion and since there were no symptoms suggestive of involvement of the optic thalamus, I do not propose to describe this case in detail.[1] In Case 10, the left optic thalamus was also invaded by the tumour.

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[1] I hope at some future period to publish reports of my other cases of intra-cranial tumour.

In none of these four cases in which the optic thalamus was invaded by a new growth were there, so far as I could detect, any definite symptoms due to the lesion in this area of grey matter, unless the paroxysms of flushings, which were very marked in Case 13, were due to this cause.

(b) *Lenticular Nucleus.*

In two cases (Case 12, which has already been detailed, and Case 24, which will afterwards be described), the lenticular nucleus was completely destroyed by a new growth. In Case 12, the motor fibres of the adjacent pyramidal tract and the island of Reil were also involved and destroyed by an acutely developed lesion. In that case there were well marked symptoms of motor paralysis on the opposite side of the body, and motor aphasia, but no symptoms indicative of a lesion of the lenticular nucleus. In Case 24, in which the left lenticular nucleus was completely replaced and destroyed by a deposit of secondary cancer, there were absolutely no symptoms indicative of the presence of a lesion in this part of the cerebral tissue.

(c) *Caudate Nucleus.*

In two cases (8 and 12) the caudate nucleus was invaded by a new growth. In Case 8, which has already been detailed, six scrofulous tumours were found in various parts of the cerebral tissue. The tumour which was present in the head of the left corpus striatum and which had entirely destroyed this portion of grey matter, did not appear to give rise to any definite symptoms. In Case 12, which has also been described, the caudate nucleus was involved along with the lenticular nucleus, the island of Reil, and the motor strands of the internal capsule. In that case the involvement of the adjacent parts produced well marked symptoms—hemiplegia on the opposite side, and motor aphasia, followed by coma. Consequently, distinctive localising symptoms due to the involvement of the head of the corpus striatum could not be expected to have been noticed.

CEREBELLUM.

In 7 cases the cerebellum was alone involved by the new growth. In 3 other cases the cerebellum, as well as other parts, was the seat of a tumour.

The following are the details of the cases:—

Case 18. (Case 4 in the Table). *Subtentorial sarcoma springing from the membranes and deeply indenting the left lateral lobe of the cerebellum; unsuspected during life.*

A. C., aged 54, female, admitted to the Newcastle-on-Tyne Infirmary on September 28, 1875, suffering from mitral stenosis, cardiac dropsy, right-sided hemiplegia (marked) of three weeks' duration.

General Symptoms. Headache; vomiting; no optic neuritis, but veins of the fundus large and tortuous, the right disc much redder than the left. Patient was in a stupid mental condition and could hardly be got to answer questions. During her stay in hospital she suffered from trembling fits, in which she was not cold.

Localising Symptoms. With the exception of the hemiplegia there were no localising symptoms—nothing to suggest a lesion of the cerebellum. It was, however, noted that when the patient attempted to stand she tumbled over, partly apparently from loss of motor power, partly from loss of control. The patient professed not to hear skull-conducted sounds in the left ear, and neither aërial nor skull-conducted sounds with the right ear.

Result. On October 21, 1875, patient died suddenly in a convulsion, in which the right side of the body appeared to be more affected than the left.

Post-mortem Appearances. A round tumour the size of a greengage plum was found below the tentorium cerebelli on the right side. It sprang from the dura and had deeply indented the lateral lobe of the cerebellum. No signs of softening or inflammation of the cerebellar tissues. A small hæmorrhage, evidently of some weeks' duration, in the extra-ventricular portion of the corpus striatum.

Marked mitral stenosis.

Remarks. In this case, so far as was ascertained, there were absolutely no symptoms suggestive of an intracranial tumour.

Case 19. (Case 8 in the Table). *Large scrofulous tumour in the right lateral lobe of the cerebellum.*

A. C., aged 9, female, admitted to the Newcastle-on-Tyne Infirmary on January 24, 1878, suffering from headache, blindness and deafness.

Previous History. Four months previously the patient had fallen and received a severe blow on the back of the head; the injury was followed by headache and vomiting. A week before admission the patient suddenly lost both sight and hearing.

General Symptoms. Headache (very severe, frontal, especially on the right side of the head). The headache was so intense that the patient, before admission to the Infirmary used to hold her head under the cold-water tap in order to relieve it. Vomiting. Double optic neuritis (marked). Giddiness not complained of.

Mental Symptoms. None. The patient, though blind and deaf, is quite bright and intelligent; she is able to distinguish her mother from other persons by the feel of her dress.

Motor Symptoms. None. The gait is natural except for the defect produced by loss of sight. No paralysis.

Knee-jerks not tested.

Sight. Absolutely blind.

Hearing. Totally deaf both to aërial and skull sounds in both ears.

Subsequent progress of the Case. Patient remained in the Infirmary until June 23, 1878, when death took place.

During her stay in hospital, she suffered from periodic attacks of severe headache and vomiting. She remained absolutely blind and deaf. She had recurring convulsions in which there was no loss of consciousness. The spasms were tonic in character and affected the head and neck, the eye-balls (which were turned upwards) and both upper extremities. Clonic spasms also occasionally occurred in the right side of the face. During the last month of her life she became stupid and apathetic, and both the contents of the bladder and rectum were evacuated involuntarily.

Post-mortem Appearances. The scalp was natural, the skull-cap very thin; it showed no signs of the former injury. The membranes were normal, the convolutions much flattened and the sulci effaced. The dura was adherent over the right lateral lobe of the cerebellum. The right lateral lobe of the cerebellum was considerably enlarged. The increase in size was due to the presence of a scrofulous tumour in its interior. The inner half of the lobe was chiefly invaded by the new growth. The other lobes and the peduncles were healthy. The ventricles were dilated. The brain substance was œdematous and soft, but otherwise normal. The internal ears and auditory nerves seemed quite healthy to the naked eye.

The bronchial and mesenteric glands were enlarged and caseous. Several deposits of miliary tubercles were present in the lungs and kidneys.

Remarks. In this case, the patient suddenly became absolutely blind and completely deaf, the intelligence and mental activity remaining quite bright.

Case 20. (Case 15 in the Table). *Four tumours in the cerebellum —three in the left, and one in the right, lateral lobe; no symptoms suggestive of cerebellar disease.*

C. McN., aged 18, seen at the Edinburgh Royal Infirmary on October 24, 1896, complaining of headache, vomiting and emaciation.

Previous History. In June of the present year, the elbow joint was excised for tubercular disease. In July the patient commenced to suffer from headache.

General Symptoms. Headache (very severe, frontal and vertical, sometimes passing through to the back of the head, increased by movement); vomiting (very frequent, incessant for the past week, occurring especially in the morning, brought on by movement); marked double optic neuritis; great emaciation; general motor weakness; marked constipation; great dilatation of the pupils.

Localising Symptoms. Slight weakness of the right hand; dynamometer, right=70, left=80. Knee-jerks equal and not exaggerated. Absolutely nothing else. No giddiness. No peculiar gait, though patient is weak on his legs. No spasms. No hemianopsia. No disturbance of sensation. No speech defects.

Mental Symptoms. The patient is inclined to be drowsy, but is intelligent. There is no impairment of memory. The patient was sent to Mr. Cotterill's wards, with a view to operation.

Subsequent Progress. Intense headache; incessant vomiting; nothing would remain on the stomach, and he had to be fed by nutrient enemata. As no treatment appeared to give relief, it was decided to trephine with the object of relieving the increased intracranial pressure.

The operation was performed by Mr. Cotterill, to whom I am indebted for the following notes of the subsequent progress of the case, on November 11, 1896. The patient was trephined over the left parietal region, the only localising symptom being slight weakness in the right hand. The intracranial pressure was greatly increased; immediately the dura was opened, the brain not only bulged through the opening, but ruptured itself. No tumour was found. A trocar was inserted in various directions into the brain, but no fluid was obtained; it was consequently concluded that the lateral ventricle was not dilated. The operation was followed for a few days by relief; the headache and vomiting were lessened, but the loss of power in the right arm increased and slight loss of power developed in the left leg. After a few days, severe headache and vomiting returned. After consultation a second operation was consequently decided upon, but great doubts were entertained as to the position at which a second trephine opening should be made. There were absolutely no mental symptoms; this seemed to exclude a lesion of the frontal lobe. There was no hemianopsia; this seemed to exclude a lesion of the occipital lobe. There was no word-deafness; this was opposed to a lesion in the left temporo-sphenoidal lobe. The fact that no fluid was obtained when a trocar was inserted deep down in the direction of the left lateral ventricle seemed to show that the ventricles were not dilated, and consequently suggested that the increased intracranial pressure was not due to a subtentorial tumour—a tumour in the cerebellum. It was, therefore, decided, by this process of exclusion, to trephine over the right temporo-sphenoidal lobe. This was accordingly done, but nothing was found. The intracranial pressure on the right side was very markedly less than on the left. The original trephine wound was again opened up. There was marked bulging of the brain at the seat of the first operation (left parietal region). A large trocar was inserted deep down into the brain and a quantity of clear fluid escaped, evidently from the left lateral ventricle. A drainage tube was introduced.

Result of Second Operation. November 25, 1896 (the day following the operation). Patient much brighter, much more sensible and intelligent, answering questions readily and correctly. Sight apparently all right. Distinct word-blindness and right-sided homonymous hemianopsia.

After this date the mental condition continued to improve, the optic neuritis became much less. The word-blindness almost completely passed off, the patient being able to read fairly well, but he continued absolutely unable to write, even to sign his name. This difficulty was not accounted for by the slight motor paralysis which was present in the right arm; it appeared to be due to destruction of fibres passing from the visual speech-centre to the motor writing-centre. The emaciation continued to increase. The second operation wound healed most satisfactorily.

January 11, 1897. The patient is very much worse. Extremely emaciated. Mentally very dull and apathetic. Answers "Aye" or "Yes" to all questions which are put to him. The scalp is markedly bulging at the seat of the original trephine wound (left parietal region).

February 7, 1897. The patient became noisy and excited. Temperature moderately elevated.

February 19. Patient died.

Post-mortem Appearances. Scalp wounds soundly healed. Bulging of the scalp in the left parietal region. A hernia cerebri projected through the trephine hole in the skull. Trephine wound on the right side of the brain normal and no bulging. Intracranial pressure greatly increased. Convolutions flattened and sulci effaced, especially over the left hemisphere. Four

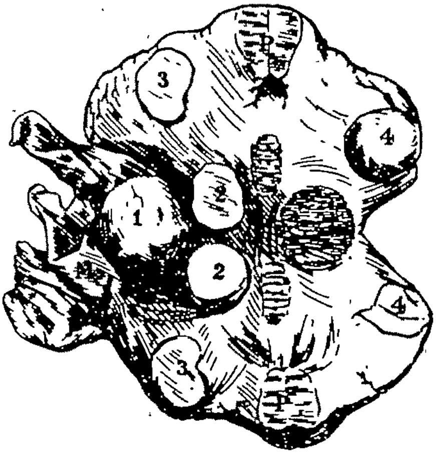

Fig. 18.

Section through the cerebellum and pons in the case of C. McN. (Case 20), showing the position of the tumours.

The letters *P P* are placed on the pons; the letter *M* on a portion of the cerebral membranes.

The figure *1* indicates tumour No. 1, which has not been divided. The figures *2*, *2* are placed on tumour 2, *3*, *3* on tumour 3, *4*, *4* on tumour 4, which have been transversely divided.

scrofulous tumours present in the cerebellum, three in the left and one in the right lateral lobe, in the following situations:—(1) a large tumour, more or less rounded in shape, $1\frac{1}{2}$ ins. by $1\frac{1}{4}$ ins. in diameter, adhering to the dura, occupying the under-surface and the back of the left lateral lobe of the cerebellum; it had caused extensive destruction both of the grey and the white matter of the cerebellum; (2) a somewhat oval tumour, measuring 1 in. by $\frac{10}{16}$ in. in diameter, situated between the first tumour and the middle lobe; it was situated in the white matter, and was in immediate contact with the large tumour (No. 1) on the one hand and with the middle lobe on the other; (3) a small kidney-shaped tumour measuring $\frac{14}{16}$ by $\frac{14}{16}$ ins. in diameter, in the anterior part of the right lateral lobe; it reached the surface and involved both the grey and white matter of the cerebellum; (4) a tumour, measuring 1 in. by $\frac{3}{4}$ ins. in diameter, in the lateral part of the right lobe; it reached the surface and involved both the grey and the white matter of the cerebellum (see fig. 18).

Remarks. This was a very remarkable case; for although there were four tumours of very considerable size in the cerebellum, there were no symptoms suggestive of cerebellar disease, except the very severe vomiting.

Case 21. (Case 24 in the Table). *Glioma and cyst of the cerebellum, involving the middle and right lateral lobes.*

A. M., aged 24, a builder, seen May 14, 1885.

Previous History. Four years ago (1880), was seized with causeless vomiting, followed by general torpor and malaise, a reeling gait, but no giddiness. One year ago (1884), suffered from severe headache, chiefly frontal, and referred to the right side of the occiput. During the present year (1885), has continued to suffer from headache and a reeling gait, but does not reel in any particular direction.

Condition on May 14, 1885. Patient complains of constant headache (frontal and right side of the occiput); is apathetic and drowsy; has an inordinate appetite; there is marked double optic neuritis; the urine contains large quantities of phosphates.

Diagnosis. A cerebellar tumour, probably gliomatous in character.

Subsequent progress of the Case. June, 1885. Continues to suffer from headache. Optic neuritis is passing into optic atrophy. Has a frequent, nervous cough. Has had several attacks of Cheyne-Stoke's respiration. Expression is vacant and staring.

Between June, 1885, *and November*, 1885, continued to suffer from headache. Had several epileptiform attacks in which the right arm and leg were sometimes the only parts which were affected. Giddiness. Temporary œdema of the eyelids. Tinnitus in the right ear and a tendency to fall backwards.

On November 3, 1885, the patient died suddenly after an attack of vomiting.

Post-mortem Appearances. Scalp, skull-cap, membranes and dura natural. Intracranial pressure greatly increased. Convolutions flattened, sulci effaced. A gliomatous tumour, in which there was a large cyst fully the size of a hen's egg, was present in the middle lobe of the cerebellum. The gliomatous tissue involved the right lateral lobe, which was extensively destroyed and atrophied. There was slight atrophy of the left lateral lobe. The pons Varolii and medulla oblongata were markedly compressed and flattened.

Case 22. (Case 27 in the Table). *Glioma of the left lateral and middle lobes of the cerebellum.*

J. J., aged 24, railway surveyor, seen May 12, 1888, suffering from headache, giddiness, vomiting, reeling gait, &c., duration 6 months. The symptoms have been much worse since the patient's marriage four months ago.

General Symptoms. Headache, very severe, chiefly frontal, at times occipital; it is of a beating character. Vomiting, frequent; usually occurs with the headache in the morning before breakfast. Occasional giddiness, especially felt if he walks fast or far. Double optic neuritis, most marked in the left eye.

Localising Symptoms. Tendency to fall to the right side. Impairment of taste in the anterior part of the tongue on the right side. Numbness on the right side of the face. Diminished tactile sensibility on the right side of the face and tongue. Knee-jerks equal and normal.

Diagnosis. A cerebellar tumour involving the central and probably the right lateral lobes; probably a glioma.

Subsequent progress of the Case. Patient did not improve under full doses of iodide of potassium. When next seen (September 6, 1888) headache and vomiting were still frequent and severe, the giddiness and reeling gait more marked, the optic neuritis more advanced. After this date he rapidly got worse, and died in November, 1888.

Post-mortem Appearances. Scalp, skull-cap and membranes normal. Convolutions much flattened and sulci effaced. A gliomatous tumour, the size of a hen's egg, was present in the cerebellum; it involved the middle and the left lateral lobes. The pons Varolii and medulla oblongata were markedly compressed and flattened.

Remarks. In this case, I expected to find the right lateral lobe involved because of the anæsthesia on the right side of the face and the loss of taste on the anterior part of the right side of the tongue.

Case 23. (Case 29 in the Table). *Gliomatous tumour of the middle and right lateral lobes of the cerebellum.*

A. B., aged 17, seen December 6, 1888, suffering from headache and vomiting, etc. Duration, one year. Supposed cause, a fall from her horse, but this was very doubtful.

General Symptoms. Headache (very severe, chiefly occipital, sometimes frontal); vomiting (frequent, usually occurring with headache first thing in the morning); giddiness (frequent, especially before breakfast before getting up); double optic neuritis (advanced in the left eye to optic atrophy). Anæmia; amenorrhœa.

Localising Symptoms. A staggering and tottering gait; a tendency to fall to the left side; complete loss of vision in the left eye, probably the result of the optic atrophy; vision in the right eye normal; knee-jerks both exaggerated, but especially the right.

No other symptoms.

Subsequent Progress. Under iodide of potassium the patient improved remarkably and, except for the blindness in the left eye, was practically well—able to walk, drive and enjoy herself, read with the right eye, etc.—during the next eighteen months. The headache and vomiting were speedily relieved, the anæmia disappeared, the giddiness became much less marked, and the gait much steadier; the menstruation returned and was regular for several months.

In *June*, 1890, the menstruation ceased, the headache returned, but there was no return of the vomiting or giddiness. The gait again became worse. Bowels became much constipated. The patient complained of general weakness and shortness of breath.

August 3, 1890 Looks remarkably well in the face; no anæmia. Complains of pain in the back of the head in the centre of the occiput. Tongue furred; bad taste in the mouth. Gait very staggering. Still tends to fall to the left side. Knee-jerks exaggerated on both sides, especially the right. Plantar reflex absent on both sides. Sight in the left eye *nil;* in the right considerably impaired. Optic atrophy present in both eyes; very advanced in the left.

In *November*, 1890, became worse. Headache, chiefly affecting the back and right side of the head. Vomiting and giddiness returned. Difficulty in swallowing developed; fluids regurgitated through the nose. Pulse remained slow, about 60.

On *December* 4, 1890, the vision became suddenly blurred; patient complained of headache; hiccough developed, and she died within the course of a few minutes.

Post-mortem Appearances. Convolutions much flattened and the sulci effaced. Lateral ventricles considerably distended. A gliomatous tumour the size of a small egg was present in the middle lobe and the adjacent part of the right lobe of the cerebellum. The medulla oblongata and pons Varolii were flattened by pressure.

Case 24. (Case 31 in the Table). *Large cancerous tumour in the right lateral lobe of the cerebellum; left lenticular nucleus completely destroyed by a round cancerous nodule; small cancerous nodule in the right ascending parietal convolution.*

M. A., aged 61, seen July 13, 1886, complaining of headache, giddiness, &c.

Previous History. Eight months ago, the left breast and axillary glands were removed for cancer. Three months ago, the patient began to complain of headache, followed by vertigo and a reeling gait. Six weeks ago she had a fit, after which there was temporary paralysis of the right side of the face. One month ago, she had a second fit or fainting, followed by marked excitement which lasted for a week and was succeeded by vomiting.

General Symptoms. Headache (persistent and very severe); vomiting (frequent); vertigo (marked); optic neuritis (intense).

Localising Symptoms. Marked vertigo. Patient says she feels as if the ceiling would fall down on her when her eyes are

The notes of Cases 25 and 26 are as follows:

Case 25. (Case 10 in the Table). *Scrofulous tumour of the left crus and cerebellum with slight tubercular meningitis.*

J. C., male, aged 1½, seen at the Edinburgh Royal Infirmary on January 24, 1890, suffering from paralysis of the right arm and leg, and paralysis of the muscles supplied by the third nerve on the left side.

General Symptoms. Little or no headache. Vomiting. No optic neuritis. Fontanelle open.

Localising Symptoms. Paralysis of the muscles supplied by the left third nerve, paralysis of the right arm and leg, and rigidity with volitional tremor in the right arm and leg.

Subsequent Progress. Under treatment, the paralysis disappeared. The child got fat, and at the end of nine months was apparently quite well. Ten months afterwards, there was a return of the vomiting, development of headache and symptoms indicative of tubercular meningitis.

The child was admitted to the Sick Children's Hospital, where he died.

Post-mortem Examination. A scrofulous tumour was found at the base of the brain in the region of the left crus cerebri; another scrofulous tumour in the cerebellum; and slight recent tubercular meningitis. I have no note of the exact position of the tumour in the cerebellum.

Remarks. The presence of a tumour in the cerebellum was not suspected during life.

Case 26. (Case 40 in the Table). *Glioma of the pons Varolii, crus cerebri and cerebellum.*

A. B., female, aged 7½, seen June 30, 1897, suffering from paralysis of the left arm and leg and paralysis of the muscles supplied by the right third nerve.

Previous History. Patient had influenza three months ago, but seemed to recover perfectly. Three weeks ago, she became more emotional than she used to be, without any obvious cause. Ten days ago, it was noticed that she had some difficulty in moving the left leg; this gradually increased. The left arm and the left side of the face gradually became affected, and some difficulty in swallowing developed.

General Symptoms. No headache when first seen; slight afterwards. Vomiting frequent. Commencing double optic neuritis. Constipation. Temperature normal.

Localising Symptoms. Paralysis of the left arm and leg and very slight of the left side of the face. Inco-ordination and volitional tremor on movement of the left arm and left leg. Ptosis of the right eyelid. Paralysis of the right external rectus muscle. Difficulty in swallowing. Knee-jerks absent.

Mental Symptoms. None. The patient is bright and intelligent.

Diagnosis. A scrofulous tumour of the right crus.

Subsequent Progress. Got rapidly worse, much thinner. Occasionally complained of slight headache. The paralysis increased. The vomiting became more frequent, the difficulty in swallowing more marked.

The patient died towards the end of August.

Post-mortem Examination. A tumour of some size was found at the base of the brain on the right side; it involved the anterior part of the right lateral lobe of the cerebellum, the right peduncle of the cerebellum, the right side of the pons, and extended up as high as the right crus. Its limits were not well defined. It was of a dull pinkish colour, of soft consistency, and on microscopical examination was found to be a glioma (the age and family history had suggested tubercle).

In addition to these cases, in which the diagnosis was verified *post-mortem*, I may detail the notes of a case in which all the characteristic symptoms of a cerebellar tumour were present, but in which operative procedure, first over one lateral lobe and then over the opposite lateral lobe of the cerebellum, failed to reveal the presence of a tumour. The notes are as follow :—

Case 27. *Typical symptoms of a cerebellar tumour; operation; no tumour found.*

S. M., female, single, 25, a servant, was admitted to the Edinburgh Royal Infirmary on January 18, 1897, suffering from headache, giddness, staggering gait and loss of vision.

Previous History. The patient was quite well until June, 1896, when the present symptoms (giddiness, difficulty in walking and headache) developed. Some months previously the menstruation had been arrested. In October, 1896, the sight became affected and the patient suffered from vomiting.

Present Condition. Well nourished; no anæmia. Temperature 97·4°

General Symptoms. Headache (severe, occipital, frontal and vertical, especially marked over the right eye and over the left side of the occiput); vomiting (frequent); giddiness (marked). Very marked double optic neuritis, passing into optic atrophy in the right eye.

Localising Symptoms. A staggering gait, with a tendency to fall sometimes to the right, sometimes to the left side, but especially to the left; this was confirmed on several occasions by independent observers. The right leg is thrown out in an incoordinate manner. Knee jerk exaggerated on the right side. No ankle clonus. Plantar reflex absent on both sides. Grasping power in the left hand, as measured by the dynamometer, 55, in the right 70. Romberg's symptom present; tends to fall to the left side when the eyes are closed. Vision in the right eye *nil;* in the left markedly diminished, $= \frac{1}{8}$ (dimness of vision no doubt due to the optic neuritis and atrophy). Nystagmus to the right and upwards; subsequently became marked when the patient looked to the left. The associated movements of the left external and right internal recti muscles weaker than the corresponding movements on the opposite side. Deaf in the left ear both to aërial and bone-conducted sounds; external ear normal. No skull tenderness. No disease of ear. No scalp swelling. Giddiness occurred in paroxysms two or three times a day and lasted from five to ten minutes at a time. Sense of smell completely absent (cause doubtful).

Mentally somewhat dull—a natural defect. Complains every now and again of a cramp-like sensation in the right side of the face.

Diagnosis. A cerebellar tumour, apparently situated in the left lateral lobe; probably a gliomatous cyst.

Subsequent Progress of the Case. Headache continued to recur and to be very severe; it was very definitely located to the left side of the occiput and over the right eye. Vomiting recurred occasionally.

On *February* 8, 1897, the patient was trephined by Mr. Cotterill over the left lateral lobe of the cerebellum. No tumour was found. The intracranial pressure was much increased. Subsequently, a second operation was performed over the right lateral lobe of the cerebellum, but no tumour was found. A good deal of bulging occurred at the site of the operation, especially on the left side. After the second operation the right side of the face and head became markedly swollen.

March 3, 1897. Patient looking very well; much brighter than before the operation. Headache almost gone. Swelling, scalp and eye, better. Has not vomited since the operation.

She remained in hospital until March 24, 1897, when she was removed by her friends, and died at home a few weeks afterwards.

No *post-mortem examination.*

Remarks. This case illustrates the great uncertainty which there is in the diagnosis of many cases of cerebellar tumour. I am still disposed to think that in it a cerebellar tumour was present, probably situated in the middle lobe and out of reach of the surgeon. The symptoms during life seemed undoubtedly to indicate a tumour in the left lateral lobe.

In Case 22, already detailed, the same difficulty of diagnosis occurred. The symptoms seemed to indicate a tumour in the right lateral lobe, whereas the *post-mortem* showed that the tumour was situated in the left lateral lobe.

But the difficulty of diagnosing cerebellar tumours is not merely confined to the uncertainty of determining in which lateral lobe the tumour is situated. In some cases in which a tumour is situated in the cerebellum, there are no cerebellar symptoms. Case 20, which has already been detailed, in which four tumours were situated in the cerebellum—three in the left and one in the right lateral lobe—is the most striking illustration which has come under my own notice. In that case there were absolutely no localising symptoms to show that the cerebellum was the seat of the lesions.

CASES OF DISTENDED VENTRICLES SIMULATING A CEREBRAL OR CEREBELLAR TUMOUR.

Further, in some cases in which the symptoms during life seem clearly to indicate the presence of a cerebral or cerebellar tumour, *post-mortem* examination shows that there is no tumour, but merely a dilated condition of the ventricular system of the brain, more especially of the fourth ventricle, the result of previous meningitis and obliteration of the foramen of Magendie. The following cases illustrate this point:—

Case 1. *Typical and characteristic symptoms of a scrofulous tumour in the cerebellum; no tumour found post-mortem, merely a dilated condition of the ventricles of the brain and old basilar meningitis.*

M. R., aged $9\frac{1}{2}$, female, admitted to the Edinburgh Royal Infirmary on October 30, 1894, suffering from headache, vomiting, double optic neuritis and paralysis of all four limbs.

Previous History. Five years ago, the patient suffered from tubercular glands in the neck. In August 1893 (fourteen months ago), the present illness commenced without obvious cause. The patient suffered from severe headache, referred to the occiput and to the right temple, and vomiting. There was no fever. Thirteen months ago, her gait became reeling and she tended to fall forwards. One year ago, she became unable to walk; and on more than one occasion, when sitting on a stool, fell backwards, apparently because she overbalanced herself or became giddy. During the summer of 1894, she had an epileptic fit.

Condition on Admission. Is well nourished. Head large; forehead narrow; occiput broad; circumference of head, $21\frac{5}{8}$ inches. Head inclined forwards. Rythmical jerking movements, both nodding and rotatory in character, of the head, on voluntary movement. Headache frequent but much less severe than in the earlier stages of the case. Vomiting occasional, every three or four days. Marked double optic neuritis passing into optic atrophy. Vision in the right eye, $\frac{6}{24}$; left, $\frac{6}{18}$. Some internal strabismus of the left eye. Nystagmoid movements of the eyes both on looking to the right and to the left. Pupils dilated and sluggish in their reaction to light. Paralysis of all four limbs, rather more marked on the left side. Legs rigid. Knee-jerks both markedly exaggerated and ankle clonus present in both legs. Volitional tremor and incoördination when patient attempts to make movements with the arms; more marked in the left than in the right arm. Some loss of control over the bladder and rectum. Memory somewhat impaired. Sensibility of the skin, hearing, taste, smell and the muscular sense normal.

Diagnosis. A scrofulous tumour of the cerebellum, probably affecting the middle and left lateral lobes, and pressing on the pons, with secondary hydrocephalus.

Subsequent Progress of the Case. Under drug treatment there was no improvement.

On *December* 24, patient was trephined by Mr. Cotterill over the left lobe of the cerebellum. The intracranial tension was greatly increased. No tumour was found. The headache and other symptoms were relieved for a time. Subsequently, the question of a second operation on the opposite right lateral lobe was considered, but deferred, as the patient's condition did not seem to warrant its performance.

On *January* 14, 1894, the patient died.

At the *Post-mortem Examination* the intra-cranial pressure was found to be greatly increased; the convolutions were flattened and the sulci effaced. A cerebellar hernia had formed at the seat of the trephined wound, and there was slight recent purulent meningitis in the immediate neighbourhood of the wound. The membranes at the base were thickened as the result of old meningitis. The foramen of Magendie was closed. The ventricular system of the brain was very greatly dilated. At the junction of the left crus cerebri with the optic thalamus, a small fibro-caseous nodule about the size of a small pea, in which there were some calcareous gritty particles, evidently an old tubercular lesion, was found.

Remarks. The symptoms in this case (good nutrition, headache, vomiting, giddiness, marked double optic neuritis, absence of fever, a staggering gait, a large head, paralysis of all four limbs, increase of the knee-jerks, jerking movements in the head and limbs on volitional effort, internal strabismus of the left eye and nystagmoid movements on looking *both* to the right and left) were typically characteristic of an intracranial tumour and seemed clearly to show that the tumour was situated in the cerebellum. Further, it should be noted that the head symptoms had commenced without any indications of meningitis, and were of long (fourteen months) duration. The case is a very remarkable one.

Only one other point need be emphasised, viz., the fact that paralysis of all four limbs, with volitional tremor, a spastic condition and exaggeration of the knee-jerks and ankle clonus, seemed undoubtedly to be due to the pressure of the dilated fourth ventricle upon the subjacent pons and medulla.

Case 2. *All the typical symptoms of a cerebellar tumour, found after death to be the result of a dilated condition of the ventricles of the brain and especially of the fourth ventricle, due to obliteration of the foramen of Magendie.*

J. M., aged 19, male, was seen at the Edinburgh Royal Infirmary on May 16, 1888, suffering from headache, vomiting, giddiness, staggering gait, &c.

Previous History. In May 1887, the patient received a head injury; he fell down several feet on to his mouth and was insensible for some hours afterwards. After recovery from this illness, he remained well until three months ago, when the present symptoms developed.

Family History. Two brothers and sisters suffered from "water in the head" and loss of eyesight.

General Symptoms. Headache (frequent and severe); vomiting; giddiness (marked); marked double optic neuritis; staggering gait (patient has on several occasions been thought to be drunk in the street); a tendency to fall backwards in the attacks of vertigo. The patient says that objects go round him from left to right. The patient is well nourished; there is no fever, and no paralysis.

Diagnosis. A cerebellar tumour, probably affecting the middle lobe, probably scrofulous or gliomatous in character.

The patient was admitted to one of the wards of the Infirmary, and died a fortnight afterwards.

Post-mortem Appearances. No cerebellar tumour. Enormous dilatation of the ventricular system of the brain; especially of the fourth ventricle, which formed a large space, the roof of which was bounded by the middle lobe of the cerebellum. The ventricular dilatation was due to thickening and adhesions of the membranes, and closure of the foramen of Magendie. There were no tubercles.

Two other cases of the same nature, verified by *post-mortem* examination, have also come under my observation; but in both of them the previous history was suggestive that the cerebral symptoms, at their commencement, were due to meningitis. I need not, therefore, detail them in full.

The cases which have just been related seem to show that in some cases it is absolutely impossible to differentiate between a cerebellar tumour and a dilated condition of the fourth and other ventricles due to blocking of the foramen of Magendie. In both of these cases, the cerebral symptoms developed without any obvious cause, and were not preceded by any symptoms indicative of meningitis. In both, the general symptoms of an intra-cranial tumour (headache, vomiting, double optic neuritis and giddiness) were present; and in both, the localising symptoms (marked vertigo and a reeling gait, etc.) were indicative of a cerebellar lesion. In Case 28, there was, in addition, paralysis of all four limbs, with rigidity, exaggeration of the reflexes and volitional tremor, such as one gets in some cases of cerebellar tumour either as the result of the lesion in the cerebellum itself, or the pressure of the cerebellar tumour on the subjacent pyramidal tracts in the pons or medulla.

I have been so much impressed with this uncertainty in diagnosis that, in some of the cases in which the symptoms of a cerebral or cerebellar tumour are present and in which the symptoms subside and the patients get well, I am disposed to think that the lesion was perhaps a dilated condition of the ventricular system of the brain, the result of obliteration of the foramen of Magendie, rather than a cerebral or cerebellar tumour which had become quiescent or had become cured under treatment. Four cases of this kind (apparent cure of a non-syphilitic cerebral tumour) have come under my own notice. In such cases, where the symptoms subside and the patient remains well, it is impossible, I think, in the present position of our knowledge, provided that there were no symptoms suggestive of meningitis in the early stages of the case, to say with certainty whether the case was one of dilated ventricles, the result of obliteration of the foramen of Magendie, or of a cerebellar tumour (scrofulous or gliomatous) which had become quiescent or healed (absorbed). That a gliomatous tumour of the cerebellum may become quiescent is shown by Case 29, which has already been detailed.[1]

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[1] In the remarks which I made at the discussion on the Treatment of Intracranial Tumours, which was introduced in the Neurological Section of the British Medical Association by Professor Ferrier, I have referred to this point in more detail (see *British Medical Journal*, vol. ii., 1898, p. 964).

AN INVESTIGATION UPON THE PLANTAR REFLEX, WITH REFERENCE TO THE SIGNIFICANCE OF ITS VARIATIONS UNDER PATHOLOGICAL CONDITIONS, INCLUDING AN ENQUIRY INTO THE ÆTIOLOGY OF ACQUIRED PES CAVUS.

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AN important and very definite variation in the plantar reflex occurring in certain pathological conditions, and having considerable clinical value, has been brought into notice by M. J. Babinski.[1] He has found that in certain cases the flexion of the toes upon the metatarsus, which is the initial movement in the normal plantar reflex, is replaced by extension of the toes upon the metatarsus. This phenomenon, which he names "le phénomène des orteils," has been found by him only in those cases where there have been lesions of the pyramidal system as evidenced clinically or by *post-mortem* investigation. An exception must be made in the case of newly-born infants, in which the plantar reflex commences with extension of the toes. Babinski explains this by the fact that in very young children the pyramidal system is incompletely developed. He claims for this sign that it never occurs in normal adults, nor in functional disease, and that of the objective signs of lesions of the pyramidal system it is the earliest to appear after the lesion, and may be the only sign present as in cases of recent hemiplegia, when the myotatic irritability is absent, or diminished; and in combined posterior and lateral sclerosis with absent knee-jerks and in Friedreichs' disease.

Van Gehuchten[3] has published an investigation of a number of cases, and has confirmed Babinski's results. My attention was first directed to the investigation of variations in the plantar reflex in January, 1898, by Sir William Gowers, who drew my attention to a case of right hemiplegia in which stimulation of the sole of the foot on the hemiplegic side produced invariably a slow extension of the great toe upon the metatarsus and no movement of the other toes or of any other muscle. The plantar reflex on the non-paralysed side was brisk and commenced with flexion of the toes.

The clinical part of this investigation is based upon :—

(1) A hundred adults examined in the medical wards of a general hospital, who being free from acute disease and presenting no sign of any lesion of the nervous system were taken as normal.

(2) A hundred children examined in the wards and out-patient department of the Hospital for Sick Children at Great Ormond Street.

(3) Three hundred cases of nervous disease that have come under my care as House Physician at the National Hospital during the last six months.

I have to thank my chiefs at the National Hospital, Dr. Hughlings Jackson, Dr. Bastian, Dr. Buzzard, Sir William Gowers, Dr. Ferrier, Dr. Beevor and Dr. Tooth for their kind permission to make use of cases under their care in the Hospital. I am also much indebted to Dr. Lees and Dr. Sydney Phillips for permission to examine the patients in their wards at St. Mary's Hospital; to Dr. Lees and Dr. Colman for permission to examine cases at the Hospital for Sick Children, Great Ormond Street, and to Mr. Stansfield Collier for permission to make use of one case.

This investigation is concerned with :—

(1) The nature and variations of the plantar reflex in normal persons.

(2) The character of the plantar reflex in diseases of the

nervous system, and the clinical value of deviations from the normal in such conditions.

(3) A theory of the causation of pes cavus in spastic states: it being possibly a result of reflex hypertonicity preponderating in certain muscles.

METHOD OF CLINICAL INVESTIGATION.

The supine position with the lower limb semi-flexed at the hip and knee and rotated out with the knee resting on a pillow so as to ensure muscular relaxation, was found to be the best for the observation of the reflex. The position of the limb was not found to have any effect upon the form of the reflex. Every precaution was used to get rid of expectant attention on the part of the person examined by distracting his attention by conversation or by the performance of some act with his hands requiring attention.

All cases in which, on repeated examination, it was found impossible to exclude volitional movements, or whose movements were not constant, or where the movements were too extensive to admit of careful investigation, were excluded from this investigation. Such cases were only rarely met with. Except in the normal cases, repeated observations were made upon each subject to ensure that the signs were constant.

Observations were also made during sleep upon many of the cases.

The plantar region was stimulated by gently scratching with the finger nail or with a soft quill, minimal stimuli being always used where possible. The effect of increasing the stimulus gradually to a heavy scratch with the nail, and the effect of painful stimulation was observed.

The order of response of the muscles in the reflex was recorded (1) by means of levers resting at one end upon that part of the muscle which bellied most during contraction, and at the other end resting upon a travelling surface; (2) by strings attached to the toes and each pulling upon one arm of a weighted bell crank lever.

The afferent path in this reflex is by the fifth lumbar and first sacral roots. I have observed that in persons where the plantar reflex was very easily elicited, stimulation of the skin over the dorsum of the foot and over the outer side of the leg (also supplied by the fifth lumbar root) produced movements precisely similar to those elicited by stimulation of the sole of the foot. The same result was never obtained from stimulating the third and fourth lumbar or second and third sacral root areas.

The response is usually confined to the lower limbs, but the involvement of the abdominal and back muscles in the response is frequently seen in children, and is much more marked on the side of stimulation.

The ease with which the plantar reflex is elicited and the degree of response varies greatly in different individuals, but the nature of the reflex is remarkably constant. I have not found it constantly absent in a healthy person. Coldness of the feet will temporarily abolish it or make it very difficult to obtain. Sensible perspiration on the feet has the same effect. Moisture does away with much of the element of friction so necessary for the production of the skin reflexes. Its effect may be readily demonstrated by moistening the back of one's hand: it becomes much less "ticklish." I have in many instances, by carefully drying the moist feet and warming the cold ones, obtained a good plantar reflex where I had failed previously. Light scratching or tickling stimuli are much more efficacious in producing the plantar reflex than more severe and painful stimuli, and the former will often succeed where the latter fail. I have not found the nature of the reflex to change in any way except in degree with different kinds of stimulation.

The irritability of the different skin regions in the sole of the foot varies greatly in individuals. I have not been able to make out definite areas where the plantar reflex could be obtained more readily, such as have been classified by Brissaud.[8]

In the clinical investigation of the plantar reflex it is very important that all the muscles of the lower limb should be observed at the moment of stimulation, because, as will be subsequently stated, the earliest response is generally in muscles of the hip, and in cases where the plantar reflex is difficult to obtain, the only response may be in those muscles.

This last phenomenon is frequently met with in functional disease; in peripheral neuritis and in tabes dorsalis.

In certain cases the reflex only appears upon the first one or two stimulations and is then absent even on the strongest excitation. This is especially apt to occur in functional cases with a slight reflex.

If the preceding points be taken into consideration, I think that the common statement that the plantar reflex is not rarely found completely absent in healthy subjects[4] will not be confirmed.

The Normal Plantar Reflex in Adults.

If a minimal stimulus be applied to the sole of the foot, a contraction of the tensor vaginæ femoris,[3] often accompanied by a less marked contraction of the adductors of the thigh and sartorius is observed in the great majority of cases.[5] With a slightly stronger stimulus flexion of the four outer toes, the movement preponderating towards the little toe appears. With increasing stimuli all the toes are flexed on the metatarsus and drawn together, the ankle is dorsiflexed and inverted; the knee is flexed and the hip is strongly flexed, adducted and rotated inwards so as to carry the knee across the opposite thigh. With still stronger stimulation violent irregular movements of the limbs occur which spread to the lower part of the trunk and to the opposite limbs.* The position of the foot at the height of a response to a moderate stimulus is shown in fig. 1. In some cases, which, however, constitute an inconsiderable minority, flexion of the four outer toes occurs with the same or even a smaller strength of stimulus than does contraction of the tensor fasciæ femoris. There is then in response to increasing stimulation of the sole of the foot, a definite order of succession in the contraction of the muscles which respond, and the contraction is more vigorous in those muscles which respond earlier than in those which react later. To illustrate this last fact the behaviour of the calf muscles may be stated. They may be felt to contract only to considerable stimulus, yet although they are much stronger muscles than the anterior tibial group, they never overcome the dorsiflexor movement, and plantar extension of the ankle is never seen in the plantar reflex of a normal person.

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* In a case of anterior poliomyelitis with complete palsy of the lower limbs, the most gentle stimulation of the sole of the foot produced a vigorous single twitch in the levator ani.

The order of contraction in all the normal cases was found as follows:—

(1) Contraction of the tensor fasciæ femoris, sartorius and adductors, and flexion of the hip.

(2) Flexion of the four outer toes.

(Sometimes 1 and 2 are simultaneous, and rarely the order is reversed.)

(3) Dorsiflexion of the ankle.

(4) Flexion and adduction of all the toes; inversion of the foot by the tibialis posticus; flexion of the knee.

(5) Contraction of calf-muscles.

(6) Contraction of quadriceps.

The early response of the tensor fasciæ femoris in the plantar reflex was first pointed out by Brissaud,[8] and it was called by him "le reflex du fascia lata."

As the response in the tensor fasciæ femoris is the first to appear, so also is it the last to disappear when the plantar reflex is diminished in normal subjects by cold, anæsthesia, and unknown factors, which cause this reflex to vary in degree from time to time in healthy subjects. I have several times found a lively response in this muscle when no other muscle reacted to stimulation of the plantar region.

The terms "early" and "late" response are here used with reference solely to the time at which a muscle reacts to stimuli, gradually increased from the minimal stimulus capable of producing a plantar reflex, and not with any reference to actual "reflex time." I have, by means of tracings taken directly from the muscles, observed that the reflex times of the several muscles in the plantar reflex only vary to an extent that can be accounted for by the different lengths of the nerves supplying them, although from the different amounts of contraction, certain muscles seem to follow others on superficial observation.

The movement produced by a moderate stimulus preponderates, as has been above explained, in the hip and ankle, and on account of the greater weight that the hip-muscles have to raise in contracting, it is most conspicuous at the ankle. This is a striking point of difference between the normal plantar reflex and that to be subsequently described in certain lesions of the central nervous system.

The economic significance of the nature of this reflex is clear. In plantigrade progression, if an irritating object come in contact with the sole of the foot, the flexors of the hip acting at greater mechanical advantage as regards range of movement than any other muscle, will be best adapted to remove the foot from the offending object; the foot is fixed by the dorsiflexion of the ankle, and the whole surface is at once removed from the ground, while the flexion of the toes and the inversion of the foot render the skin of the plantar region lax, so that any sharp object will penetrate less readily.

For the sake of brevity in this communication I propose to call this normal form of plantar reflex characterised by flexion of the toes and marked early action of the tensor fasciæ femoris as the "flexor response."

The Crossed Plantar Reflex.

A crossed plantar reflex can usually be obtained in cases where the plantar reflex is marked. It consists of a slight movement of flexion of the toes, especially of the great toe, with slight dorsiflexion of the ankle.

Usually a much stronger stimulus is necessary to produce the crossed plantar reflex than the direct, but this is not always so; sometimes the minimal stimulus required to produce the plantar reflex will evoke a distinct crossed reflex.

The Normal Plantar Reflex of Infants.

The response is very brisk, and differs very markedly from the adult reflex. The earliest response is in the great toe, which is drawn back. This is followed by extension and spreading out of all the toes with eversion of the foot and dorsiflexion of the ankle, and subsequently flexion of the hip and knee. Strong stimulation causes a general, irregular movement of the limbs and trunk. The crossed plantar reflex, when I have been able definitely to obtain one, has consisted of extension of the toes.

This form of reflex, with the widely-spread, drawn-back toes and the late response of hip-muscles contrasts most markedly with the adult form, with the contracted, flexed toes, inverted foot and the early hip response. I propose to use the term "infantile response" for this type of plantar reflex.

It may be remarked here that this form of plantar reflex is precisely similar to the plantar reflex of such monkeys as I have examined, and may be considered a more primitive type. To this point I shall recur subsequently.

The infantile response persists until the child becomes able to walk, when it is gradually replaced by the flexor response. I have observed several cases in the transition period, and in these children sometimes one and sometimes the other form of response occurred at the same examination, or a mixed response of flexion of the outer toes with marked extension of the great toe occurred.

The age at which the change occurs is generally between the second and third year. I have met with the typical adult response in children of two years old, who were particularly forward and "strong on their legs."

In weakly, and especially in rickety children, the infantile response may be seen as late as the age of four years.

It may, then, be stated that with the establishment of complete cerebral control over the lower limbs the adult form of response to the plantar reflex replaces the infantile response.

The Plantar Reflex during Sleep.

During sleep the plantar reflex is diminished, and in infants and adults the infantile and flexor responses occur respectively, but in some children up to the age of twelve years who presented the adult flexor response when awake I have observed a most interesting phenomenon. During deep sleep there was a typical infantile response, with the extension and spreading of the toes and eversion of the foot. With repeated stimulation complicated co-ordinated movements directed towards the removal of the cause of irritation were noticed. It seemed as if some higher mechanism had been roused into action. Further irritation of the foot caused the child to awake, and directly he did so the normal adult plantar reflex occurred on stimulation.

In these cases the temporary loss of cerebral influence over the spinal cord during sleep was accompanied by a reversion to the primitive infantile response, which disappeared and was replaced immediately by the adult response on awakening.

In children between the ages of six and twelve years this peculiarity was only found in a minority of the subjects examined.

The Plantar Reflex in Pathological Conditions.

(1) Lesions of the pyramidal system.

An alteration in the form of the plantar reflex in these lesions was first described by Babinski.[1] He found that if in the plantar reflex, extension of the toes, especially of the great toe, upon the metatarsus occurred, this extension of the toes was pathognomonic of a lesion of the pyramidal system. To this rule he made two exceptions: (1) In newly-born infants he noticed that the infantile response was constant; (2) In cases of total transverse lesions of the cord he was unable to obtain any plantar reflex.

He named this sign "le phénomène des orteils," and states that he has never found it in healthy subjects or in functional cases, but only where there was clinical evidence of a lesion of the pyramidal system, and conversely that in lesions of the pyramidal system, with the exception of total transverse lesions of the spinal cord, this sign almost invariably occurs. His pathological investigations entirely confirmed this statement.

Van Gehuchten[2] has confirmed these results.

I find that the form of plantar reflex in lesions of the pyramidal system, whilst resembling the infantile response in many respects, differs in a few points. In a well-marked case, the whole response is more deliberate than in the flexor response or the infantile response, and appears with much more certainty than does the flexor response to each stimulation. Extension of the great toe precedes all other movement. It is followed by extension of the other toes and by dorsiflexion and inversion of the ankle. The tensor fasciæ femoris does not contract early. The tibialis posticus and anticus and peroneus longus contract strongly, and fix the ankle, and a temporary increase of the plantar arch is often noticed. The small amount of movement at the ankle in the reflex from this cause is conspicuous, and contrasts with the brisk movement of the ankle in the normal reflex. There is often a tendency of certain muscles to remain contracted after the reflex, especially the extensor proprius hallucis, reminding one of the cataleptoid reflexes observed by Sherrington in paraplegic monkeys.[3]

Just as the response of extension of the great toe is the first to appear, so when the reflex is very sluggish the extensor proprius hallucis may be the only muscle to respond even to strong stimulation.

I propose to use the term "extensor" response for this form of reflex.

This extensor response is often more easily elicited by stimulation of the outer part of the sole, whereas the flexor response is usually more easily obtained by stimulating the inner part.

The position of the foot at the height of a moderate extension response is depicted in fig. 2.

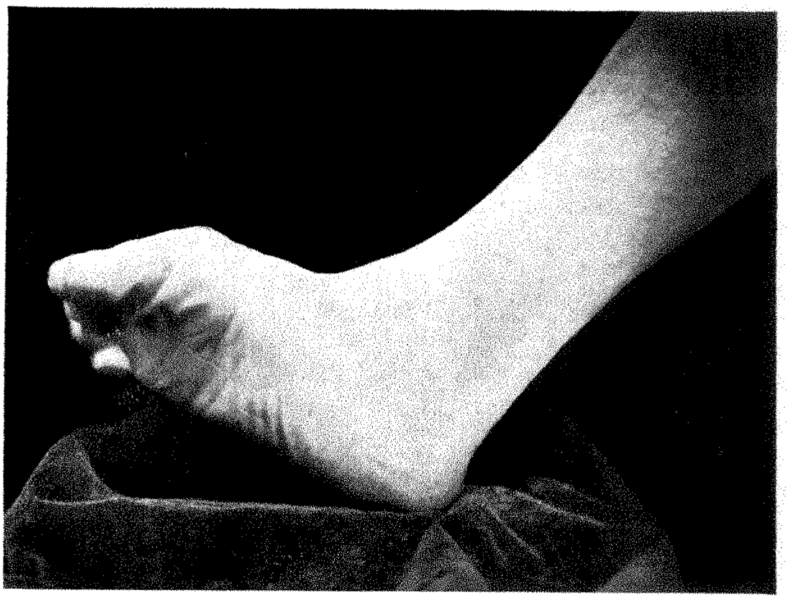

FIG. 1.

The position of the foot of a healthy adult at the height of a flexor response. The flexion and adduction of the toes, and the dorsiflexion and inversion of the ankle are well shown. (From an instantaneous photograph.)

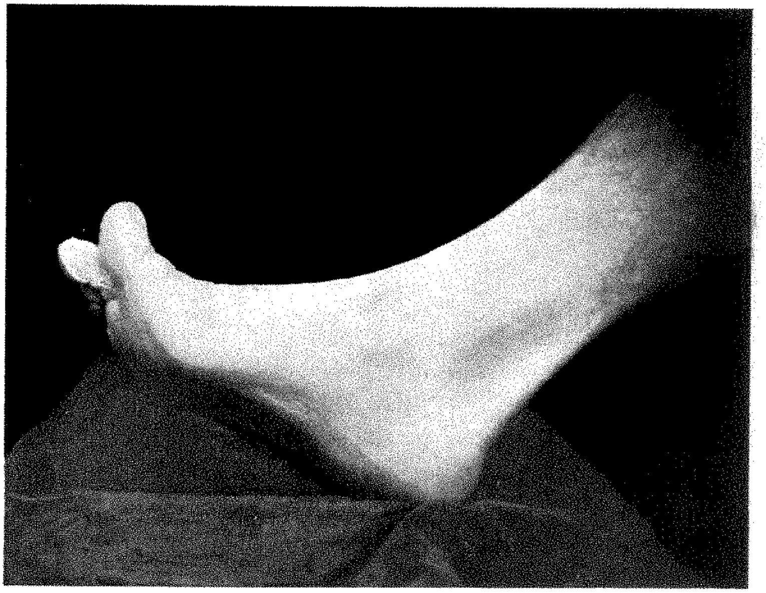

FIG. 2.

The position of the foot at the height of a moderate extensor response. The increase of the plantar arch and the extension of the toes, especially of the hallux, are well shown. From an instantaneous photograph. The case was one of early disseminated sclerosis.

In the following table the chief characteristics of the three forms of response are contrasted.

	NORMAL.	EXTENSOR RESPONSE.	INFANTILE RESPONSE.
Movement	Quick	Often deliberate	Quick
Muscle first to contract with a minimal stimulus	Tensor fasciæ femoris	Ext. prop. hall.	Ext. of toes
Certainty of response to each stimulus	Less certain	Certain	Less certain
Position of toes	Flexion; adduction	Extension; spreading	Extension; spreading
Obtained more easily by stimulating	Inner part of the sole	Outer part of the sole	
Movement of ankle	Dorsiflexion and inversion, both conspicuous	Dorsiflexion and inversion, both slight	Dorsiflexion and eversion, both conspicuous

According as the lesion of the pyramidal system be partial, the flexor and extensor responses may be combined in the plantar reflex. The following are common clinical variations:—

(1) Extension of great toe with flexion of four outer toes.

(2) Slight flexion of all toes, followed by slow, strong extension.

(3) Contraction of tensor fasciæ femoris, and of extensor proprius hallucis with the minimal stimulus.

(4) Stimulation of the sole may sometimes produce the flexor, and sometimes the extensor response.

Especial care must be taken in investigating the plantar reflex that a movement of dorsiflexion of the ankle is not mistaken for a movement of extension of the great toe. The movement at the metatarso-phalangeal joint must be carefully inspected to obviate this source of error.

The Crossed Plantar Reflex Associated with the Extensor Response.

The cases showing the extensor response almost invariably present slight flexion of the toes, preponderating in the great toe as the crossed plantar reflex, whether the condition present is a hemiplegia or a paraplegia.

I have met with slight extension of the toes—chiefly of the outer toes—as a crossed plantar reflex in two cases only, both cases of severe spastic paraplegia.

The clinical and pathological results obtained in this investigation have, for the most part, confirmed Babinski's conclusions, and exceptions to his rule that the extensor response indicates a lesion of the pyramidal system have been found so few as to "prove the rule."

(1) *Total Transverse Lesion of the Cord.*

In three cases of total transverse lesion of the cord I have found the extensor response present. Bastian[7] states that in his cases slight movements of the toes on stimulating the sole were the only reflex phenomena present, but does not state the nature of the movement.

Case I.—R. L., labourer, aged 52 years, was admitted into St. Mary's Hospital, under Mr. Stansfield Collier, on September 26, 1898, with a severe injury to the dorsal spine, caused through a fall a few hours previously. He was completely paraplegic, and the knee-jerks were absent. A laminectomy was at once performed, and the spinal cord was found completely severed at the level of the fifth dorsal vertebra. Twenty hours later stimulation of the sole of either foot produced a sluggish extension of all the toes, especially the great toe, and this sign persisted till his death three days later. The response was absolutely confined to the foot. The knee-jerks were persistently absent.

Case II.—A. G., aged 50 years, was admitted into the National Hospital under Dr. Buzzard suffering with cancer of the dorsal vertebræ secondary to a scirrhus of the left breast, which had been removed. She had complete flaccid paraplegia and complete anæsthesia as high as the eleventh dorsal root level. The knee-jerks were absent and the sphincters completely incontinent. Up to the time of writing, these physical signs have been constant, except that the anæsthesia is creeping upwards. She has always shown a moderate extensor response at the plantar reflex.

(Since writing the above the patient, A. G., died. At the autopsy a mass of new growth was found compressing the spinal cord at the level of the seventh dorsal nerve-root. The cord was narrowed to the size of a crow-quill and its substance was semi-diffluent at this point.)

Case III.—A. E., a laundress, aged 20 years, was admitted into the National Hospital under Sir William Gowers on Sept. 16, 1898, suffering with acute syphilitic transverse myelitis of six days' duration. She had complete flaccid paraplegia, and absolute anæsthesia up to the tenth dorsal root level; complete incontinence and loss of knee-jerks. The plantar reflex was a marked slow extension of the hallux alone. The knee-jerks returned ten days later, and some movement fifteen days later.

Although there was no anatomical proof of a total transverse lesion in the last two cases, there was full clinical evidence of a physiological total transverse lesion.

(2) *Myelitis (including Compression Paraplegia).*

Of thirty-six cases repeatedly examined, thirty-four always showed a marked extensor response. In one case of twenty years' duration there was great organic contracture of the calf muscles, so that the ankles were fixed in a position of plantar extension and could not be passively dorsiflexed; the toes were fixed in a position of flexion and could not be extended. The faradic excitability of the anterior tibial muscles was absent. The plantar reflex was confined to a flexion of all the toes.

In one case of cervical myelitis there was associated atrophic palsy of the extensors of the toes and loss of the deep reflexes. The plantar reflex consisted in a flexion of the toes.

The two following cases exemplify the return of the plantar reflex to the normal on recovery.

Case IV.—Percy C., aged 5 years, was admitted into the National Hospital under Dr. Tooth on April 15, 1898, with symptoms of spinal caries of six weeks' duration and gradually increasing paraplegia of three weeks' duration, with hesitating micturition; increased knee-jerks and double foot clonus. The plantar reflexes were very strong extensor responses.

On May 17, having been treated with rest and extension since admission, he was completely paraplegic. On May 17 Mr. Horsley performed laminectomy and removed a large amount of gelatinous tubercular material that was found pressing upon the theca.

On June 7 he began to move his legs. The wound was healed on June 25.

On October 20 he could walk well, and with the exception of some increase of the knee-jerk, all his symptoms of paraplegia had disappeared. The plantar reflex was sometimes an extensor, and sometimes a flexor response.

On October 30 the plantar reflexes were constantly flexor responses. He could walk and run naturally.

Case V.—J. P., aged 34 years, an engineer, was admitted into the National Hospital under Dr. Beevor in November, 1898, with spinal caries and slight weakness of the legs. Movements of the legs were well performed, but with a feeling of stiffness. The knee-jerks were increased, and there was a little foot clonus. He had occasional reflex flexor spasms in the legs. The plantar reflexes were marked extensor responses; the extensor proprius hallucis contracting to a much slighter stimulus than did the other muscles concerned in the response.

After a fortnight's rest in an extension apparatus, the feeling of stiffness, increased deep reflexes and flexor spasm had entirely disappeared. The plantar reflex, after showing sometimes an extensor response and sometimes a flexor response, became constantly a flexor response.

In these cases the extensor response was the last of the "spastic" signs to disappear.

(3) *Disseminated Sclerosis.*

Of thirty cases, twenty-eight showed an extensor response on both sides. In one case in which the signs were limited to the right limbs, there was an extensor response on the right side and a flexor response on the left.

In one case in which the knee-jerks were diminished and the chief symptom ataxy, there was a flexor response on both sides.

In five cases of paraplegia, where the symptoms had been entirely those of functional disease and a diagnosis of functional paraplegia was made, symptoms of organic disease, such as diplopia, sphincter trouble, erythromelalgia, girdle sensation, &c., subsequently appeared, and the diagnosis was changed to (?) disseminated sclerosis.

In two of the cases the onset of unequivocal signs of organic disease was accompanied by a change from the flexor to the extensor response and persistence of the latter.

In two cases the flexor response persisted, though signs of extensive organic disease developed.

In one case the tensor fasciæ femoris alone responded in the plantar reflex.

In the differential diagnosis between functional and organic hemiplegias and paraplegias in adults, the presence of an extensor response is a most valuable sign of organic disease, such as is not furnished by increase of the knee-jerks or by the less persistent forms of foot-clonus. The presence of a flexor response, however, is compatible with the presence of organic disease.

(4) *Hemiplegia.*

Of thirty-six cases of organic hemiplegia, twenty-eight gave an extensor response on the paralysed side and a flexor response on the sound side. The reflexes were found in some cases very brisk, in others very difficult to obtain. The cases with brisk and those with sluggish reflexes were classified and compared, but no general fact as to the cause of the difference was elicited.

In three cases the extensor response was found on both sides, and an autopsy in one of them—a case of right hemiplegia—revealed degenerative changes in both hemispheres.

In one case of eight weeks' duration the plantar reflex was entirely absent on the paralysed side, a flexor response being present on the sound side.

In four cases the flexor response was found on both sides. In one of them the leg had entirely escaped the paralysis. In the other three the flexor response was more marked on the paralysed side and was very atypical, consisting of a vigorous flexion of all the toes. In these three cases the appearance of the foot on the hemiplegic side was peculiar; the foot was dropped, and the toes were, when at rest, bent strongly towards the sole of the foot, the line of the inner side of the foot from the tip of the great toe to the heel forming the chord of a circle. This position of the foot is the opposite to that of pes cavus, which is not rarely met with in cases where the pyramidal system is damaged, and which will be subsequently described as having a most important connection with the extensor response.

I have no explanation to offer for the peculiarities of the plantar reflex in these three exceptional cases.

(5) *Friedreich's Disease.*

Of six cases all showed a marked extensor response. Four of the cases had marked pes cavus, and the knee-jerks were absent. The others had slight pes cavus, and the knee-jerks were just obtainable.

Clinically, the only sign of the affection of the lateral columns is the extensor response in the plantar reflex and the pes cavus.

(6) *Syringomyelia.*

Of three typical cases all showed a marked extensor response.

(7) *Amyotrophic Lateral Sclerosis.*

Of three cases all showed an extensor response.

(8) *Bulbar Palsy and Progressive Muscular Atrophy.*

The cases in which the deep reflexes in the lower limbs were increased showed the extensor response. Where the lower limbs were normal the flexor response was present.

Epilepsy.

Of forty cases thirty-eight showed the flexor response. After every fit of severe convulsions lasting any length of time the extensor response was found present, and lasting some time.

In one patient, who suffered from periodic groups of attacks of severe general convulsions, the flexor response was constantly present when he was free from attacks. During a period of forty hours he had fourteen severe fits; the extensor response was always present and persisted for seven hours after the last attack, when the flexor response returned.

The extensor response, as a rule, was present for from five to ten minutes after a general convulsion.

In cases of hemi-epilepsy, not associated with hemiplegia, the extensor response was only present after the fits on the convulsed side.

Where the general convulsions were of very brief duration often no change in the plantar reflex was observed.

Cases of Jacksonian epilepsy affecting the foot always presented an extensor response for a short time after the fit.

The following two cases of epilepsy were exceptional:—

Case VI.—A. S., aged 20 years, under the care of Dr. Bastian, had suffered with right hemi-epilepsy since a severe fit at the age of two years. The right arm and leg were distinctly smaller than the left, and the movements, although all well performed, were slightly weaker than those on the left side. The gait was natural, and the right knee-jerk was only slightly more lively than the left. She had had no fit for six weeks before admission. The right plantar reflex was constantly an extensor response, the left a flexor response.

In this case a lesion of the left cortex had probably occurred at the time of the first fit. The extensor response was the most evident sign of the hemiplegia, the weakness and impaired development being so slight as to be easily overlooked.

Case VII.—J. G., aged 28 years, under the care of Dr. Ferrier, had suffered for two years with slight general convulsions.

She had not had infantile convulsions. There was no physical sign of organic disease, except that an extensor response was constantly obtained in the left foot, a flexor response in the right.

I look upon this case with suspicion, and think that it may possibly be a case of cerebral tumour.

Many patients have presented in the out-patient department of this hospital as cases of idiopathic epilepsy, who for years showed no sign or symptom of organic disease, and subsequently developed unequivocal signs of intracranial tumour. Several such cases subsequently examined in the *post-mortem* room have shown neoplasms in the anterior parts of the hemispheres.

I would suggest that the presence of a constant extensor response, since it may be the earliest sign of a damage to the pyramidal system, may be of great value in the early recognition of some of these cases.

In the following case of cerebral tumour, commencing with epilepsy, the presence of a unilateral extensor response was of great clinical value.

Case VIII.—Annie S., aged 12 years, was admitted on Sept. 22, 1898, into the National Hospital, under the care of Dr. Buzzard.

Four months before admission, after an attack of influenza, she began to have frequent attacks of "petit mal." She would suddenly turn pale and look strange, and say "I feel so funny." A fortnight later it was noticed that in some of the attacks the left arm twitched.

She was sent to the Meath Home for Epileptics, and when admitted there she was constantly falling asleep at all times of the day, though quite bright and natural when awake. It was then noticed that she did not use the left side of her face in talking so well as the right.

A month before admission her sight began to fail rapidly. A fortnight later paroxysms of vomiting began for the first time in her illness. She had no headache until two days before admission. On admission she was obviously very ill. Her mental state was intelligent. Speech and articulation were normal. She had frequent Jacksonian attacks, beginning sometimes in the left face, sometimes in the right face, sometimes in the right hand and sometimes in the left hand, remaining always confined to the side on which the attack commenced. She was quite conscious and able to speak during the attacks. Taste, smell and hearing were normal. There was intense optic neuritis showing a commencing subsidence into atrophy. There was absolutely no light perception. There was complete palsy of the right third and sixth nerves and partial palsy of the left third and sixth nerves. There was very slight weakness of the left lower face and of the left arm. There was absolutely no weakness of the legs, and her gait was natural. There was no localised cranial pain or tenderness. Sensation was natural. The knee, wrist and elbow jerks were absent and were never obtained up till her death. The plantar reflex on the right side was a marked flexor response, that on the left side a vigorous extensor response. This condition of the plantar reflex persisted till the day before death, two months later, when she became deeply comatose, and the extensor response was present on both sides, but was much more marked on the left side.

A month aftor her admission she dragged the left foot slightly in walking, but after this the hemiplegia did not progress.

The autopsy revealed an infiltrating tumour of the white substance of the right temporo-spenoidal lobe extending as far as the right capsule. A tongue of new growth extended over the right crus and was pressing upon the right third nerve.

In this case the early attacks of "petit mal," the somnolence and the Jacksonian attacks indicated a lesion of the hemispheres, but did not suggest which hemisphere was involved.

The slight hemiplegic symptoms in the left face and arm confirmed by the extensor response in the left foot gave an accurate indication as to the side of the lesion.

Cerebral Tumour.

Sixteen cases were examined in which there were no physical signs of any lesion of the pyramidal system. In all of these the flexor response was present.

Cerebellar Tumour.

Of three cases all showed a flexor response.

Functional Disease.

Of thirty-five cases, fifteen showed a moderate flexor response. In three cases there was an extremely brisk flexor response on the least stimulation of the sole. In ten cases the flexor response was elicited with difficulty.

In seven cases the plantar reflex had been recorded in the notes as absent, and in two of them this absence had been repeatedly noticed for years, but in all of these cases there was a distinct contraction of the tensor fasciæ femoris on stimulating the sole. The reflex only followed the first few stimulations, and then disappeared. It was apparently very easily tired out, for it always reappeared after a few minutes' rest.

The absence of the plantar reflex in cases of functional paraplegia where there is no anæsthesia of the feet has been brought forward by Dr. Buzzard[8] as characteristic of that condition. So far as the absence of response in the foot is concerned, it occurred in 20 per cent. of all cases examined and almost invariably in functional paraplegia, but I did not meet with a functional case in which there was entire and constant absence of response in the muscles of the hip.

Paralysis Agitans.

Of ten cases, the flexor response occurred in all, and the reflex was sluggish.

Tabes Dorsalis.

Of twenty-five cases, eight showed an entire and persistent absence of any response. In three cases the tensor fasciæ femoris alone responded. In five cases an attempt to elicit the plantar reflex produced irregular movements of the toes and foot, often of considerable range lasting some time. In the remaining cases the flexor response was present, in some cases much delayed, in some cases brisk, in others sluggish. Anæsthesia of the feet seemed to have no connection with the presence or absence of the reflex. In one case where there was long-standing complete anæsthesia to all forms below the knees the flexor response was particularly brisk.

The extensor response was never met with.

In the following case the presence of a marked extensor response furnished a valuable suggestion as to the diagnosis.

Mary C., aged 35 years, married, was admitted into the National Hospital under Dr. Ferrier on September 28, 1898, complaining of weakness of the legs and inability to walk. Her previous health had been good. Her first child was born dead at six months, and her only other child was alive and healthy. Her illness commenced eighteen months before admission with subjective stiffness in the calves, tingling of the feet and a tight girdle sensation. Nine months before admission she dragged both feet in walking, and had slight precipitancy of micturition. Six weeks before admission she became entirely unable to walk alone.

The pupils and cranial nerves, optic discs and special senses were normal. There was slight blunting of sensibility over the feet as high as the ankles, some loss of sense of position at ankles and knees. She complained of aching pains in the legs. There was no wasting of the lower extremities and all movements were performed with moderate power. There was no hypotonia. There was great ataxy in the legs and marked Romberg's sign. In walking the feet were poorly lifted, but did not scrape the ground. The knee-jerks were absent. There was some precipitancy of micturition. The plantar reflex on both sides was a marked extensor response.

The case presented at first sight as one of atypical tabes but there was a definite history that she had dragged her feet in walking before she became very ataxic. This was not a symptom of posterior sclerosis.

In the cases of tabes examined by Babinski, Van Gehuchten and myself, the extensor response was never met with.

Babinski states that in his cases presenting the extensor response every autopsy revealed a lesion of the pyramidal system, and the same result had been obtained from autopsies upon my cases.

From these facts the diagnosis of postero-lateral sclerosis was in this case strongly suggested.

(Since writing the above two patients who presented as atypical cases of tabes, the knee-jerks being lost and the extensor response present, as in this case, have died in the

National Hospital. Autopsies upon both cases revealed marked degeneration in both the posterior and lateral columns of the spinal cord.)

Multiple Peripheral Neuritis.

Of fifteen cases nine gave a flexor response, generally sluggish. In three severe cases the plantar reflex was entirely absent while the patients were under observation. Three cases showed a response confined to the tensor fasciæ femoris.

Chorea.

In twenty cases (including three cases of Huntingdon's chorea) a normal flexor response was found.

Anterior Poliomyelitis and Myopathies.

In twenty cases of acute poliomyelitis, occurring after the patients had learnt to walk, the flexor response was met with. Where the muscles concerned in the response were involved in the palsy, the response was diminished or lost in proportion to the degree of paralysis.

In six cases of myopathy a similar result was obtained. One case, however, was exceptional. This was a very typical case of pseudo-hypertrophic palsy in a boy of nine years old, who had learnt to walk when eighteen months old, and had been particularly strong and active upon his legs till the age of four years, when his symptoms commenced. In this boy a marked infantile response was always present.

In cases of *neurasthenia* and *sciatica* the plantar reflexes were found normal.

THE INFLUENCE OF STRYCHNINE AND TETANUS TOXINE ON THE PLANTAR REFLEX.

M. Babinski has recorded a case of strychnine poisoning in which "le phénomène des orteils" was present and disappeared soon after recovery.

Several adults who presented the flexor response have been treated under my care with increasing doses of a solution of nitrate of strychnine administered hypodermically and I have found that when large doses—one-sixth to one-third grain—are given, the form of the plantar reflex becomes changed, and resembles that found in lesions of the pyramidal system.

The change in the reflex was noticeable about five minutes after the injection, and persisted for about half-an-hour. No discomfort beyond a slight feeling of general stiffness on movement was experienced by the patients after the injection.

The same change persisting many weeks after recovery was observed in a case of tetanus recently in the National Hospital.

Case X.—S. B., a healthy boy, aged 5 years, was admitted under the care of Dr. Hughlings Jackson, on September 6, 1898. Tetanic symptoms had set in ten days after a wound on the forehead. The spasms were severe and confined to the head, neck, and upper limbs. They ceased on the tenth day after admission, and he became rapidly convalescent. During the stage of acute symptoms, and for a month afterwards, a strong, deliberate extensor response was invariably the result of stimulating the sole of the foot. On October 24 sometimes a flexor response, and sometimes an extensor response, with a diminished contraction of the tensor fasciæ femoris were obtained. After November 1 no extensor response was obtained, a marked flexor response being present, with a very lively action of the tensor fasciæ femoris. This form of reflex persisted as long as he was under observation.

Both strychnine and tetanus poison increase the reflex excitability of the spinal cord, and the cerebral control is thereby relatively lessened. The increased reflex excitability was in these cases accompanied by a return of the form of plantar reflex to the infantile type.

THE ÆTIOLOGY OF ACQUIRED PES CAVUS IN SPASTIC CONDITIONS.

In cases of Friedreich's disease, in the family type of primary lateral sclerosis, in lesions of the spinal cord producing a spastic condition of the lower extremities, and in cases of hemiplegia (especially in children and young people) a deformity of the foot known as pes cavus is sometimes met with. In well-marked pes cavus the whole foot is dropped; the toes, especially the great toe, are retracted, forming an angle with the metatarsus. The metatarsus itself is pulled down in front, and with the anterior part of the tarsus forms an angle with the posterior part of the tarsus, so that the inner border of the foot has an outline somewhat resembling that of the letter Z.[11] The plantar arch is increased and the foot is inverted. In long-standing cases the metarso-tarsus is often structurally shortened.

Several explanations have been brought forward to account for the development of pes cavus. Duchenne[9] considered that it is due to weakness or paralysis of the interrossei, combined with weakness of the dorsiflexors of the ankle, and stated that weakness of these muscles and an altered electrical excitability may be found in them. He considered pes cavus as a similar condition with a like cause to "main en griffe."

Golding Bird[10] also considers this explanation valid.

If a hand presenting "main en griffe," with its paralysed and atrophied muscles, structural rigidity, and marked rigid flexion of the interphalangeal joints be compared with a foot showing marked pes cavus in Friedreich's disease, where there is no wasting nor paralysis, no contraction of tendons, no rigid flexion of the interphalangeal joints, and no alteration of electrical excitability in the muscles, the resemblance between the two will be found superficial rather than real.

I have carefully examined many cases of pes cavus, and have been unable to find any relative weakness of these muscles, or any change in their electrical excitability.

Duchenne's explanation applied to the pes cavus of spastic states is, I think, untenable, and does not account for the inversion of the foot, nor adequately for the increase of the plantar arch.

Adams,[12] in 1864, considered the condition to be produced by spasm in certain muscles.

Barwell,[13] in a recent paper, considers Duchenne's explanation will not account for most of the cases. After discussing the congenital and paralytic forms, he says, "a third class of pes cavus is due to spastic tension in the long peroneal muscle. Though I cannot determine the cause of this contraction, I have more than once demonstrated its presence."

I have examined a large number of cases of hemiplegia and paraplegia of long duration, with spastic lower extremities, and have found in all of them which showed an extensor response in the plantar reflex a tendency to that position of the foot known as pes cavus. The results were most striking in cases of hemiplegia, where the non-affected foot could be taken as the normal. (Accurate measurements of the length of the plantar arch, &c., were taken by means of a flat rule placed against the sole of the foot and a divider working at right angles to the rule. The measurements were also taken from accurate plaster casts of the same feet in some cases.)

I have been able to watch the development of pes cavus from a normal foot in three cases. The feet depicted in figs. 3 and 4 were those from a case of spinal caries with paraplegia, under the care of Dr. Bastian. This patient was admitted into the National Hospital with a condition of slight spastic paraplegia, and her feet showed no deformity; she became absolutely paraplegic, and pes cavus slowly developed. The photograph was taken a year after the onset of the paraplegia.

I have also had the opportunity of examining four cases of early Friedreich's disease with commencing pes cavus. In all these cases the earliest signs of deformity was retraction of the great toe, and the second noticeable event was spasm of the tibialis posticus and peroneus longus muscles, as evidenced by the constant standing out of their tendons behind the internal and external malleoli respectively.

In a well-marked case, the standing out of the tendons of the extensor proprius hallucis, tibialis posticus, and peroneus longus is most noticeable, and is well depicted in figs. 4 and 5 (in this case there was no structural rigidity; the deformity could be easily reduced by force). Exception must here be made in cases of late Friedreich's disease where considerable hypotonia has developed.

A condition of muscular spasm preponderating in the extensors of the toes, tibialis posticus and peroneus longus would produce a position of the foot similar to pes cavus. The toes would be extended, the forward part of the metatarsus would be drawn down by the tendon of the peroneus longus attached to the base of the first metatarsal bone, and by the prolongation of the tibialis posticus to the middle three metatarsal bones. Both of these muscles increase the plantar arch, and both plant-extend the foot. Inversion of the foot would result, as the tibialis posticus is a stronger muscle than the peroneus longus, and inversion of the foot a stronger movement than eversion.

Isolated paralysis of the tibialis posticus produces entire loss of the antero-posterior plantar arch and eversion of the foot. (Erichsen.)[14]

I would suggest that spasm preponderating in the muscles is the correct anatomical explanation of acquired pes cavus, and there is clinical evidence that such spasm does actually exist in these cases.

A physiological explanation for the occurrence of such spasm must be sought for, and it will be found in the extensor response in the plantar reflex. Pes cavus occurs not infrequently in diseases in which a lesion of the pyramidal system occurs, and I think that a tendency to pes cavus may be found in nearly all such cases if they be of long standing. The extensor response is almost always present in such cases, and is especially marked when any degree of pes cavus occurs.

The tone of the muscles supplied by a spinal segment is dependent upon the reflex arc of that segment, and may be described as the response on the efferent side to the continuous afferent impressions reaching the segment by its afferent nerves.

In the absence of the control of higher centres the physiological capacity for reflex response of the spinal segment increases, and with it the muscular tone which may go on to rigidity. The efferent impulses leaving the

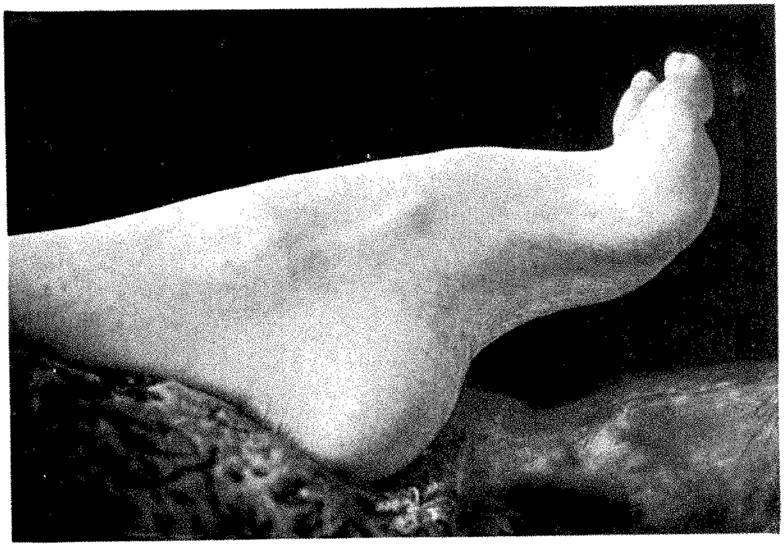

Fig. 3.

The appearance of the left foot at rest from the internal aspect in a case of spinal caries under the care of Dr. Bastian. The pes cavus had developed while the patient was in hospital. The standing out of the tibialis posticus tendon is seen. (From a photograph.)

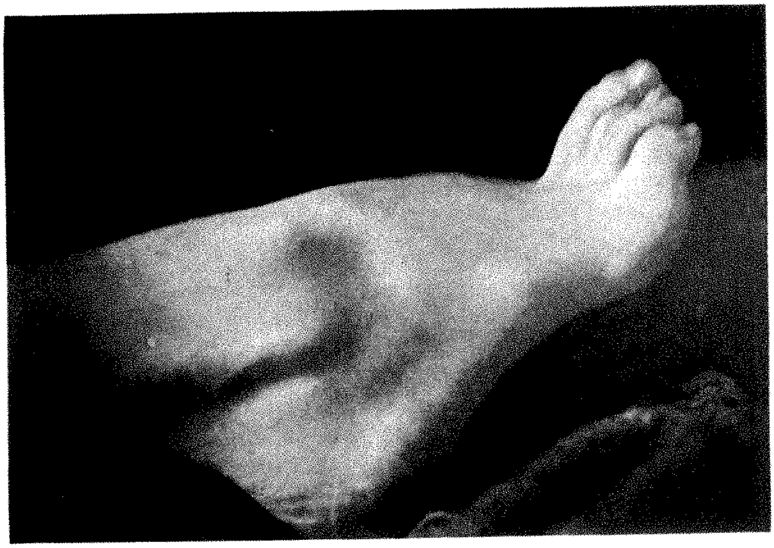

Fig. 4.

The right foot from the same case as Fig. 3, seen from the outer side, showing the standing out of the tendon of the peroneus longus.

spinal segment, in the absence of control from higher centres, will be distributed to muscles in the same pattern as the response to the superficial reflex connected with that segment.

The form of the superficial reflex in the foot, when the higher centres are cut off, is, extension of the toes, with slight inversion and dorsiflexion of the foot, and increase of the plantar arch, and marked action of the tibialis posticus and anticus and peroneus longus. The pattern of muscular tone in the same condition is this extensor response stereotyped; there is relative hypertonicity in the extensors of the toes, in the tibialis posticus and peroneus longus, and to a less degree in the tibialis anticus. This relative hypertonicity, if persisting for a long time, will cause the foot to assume the position of more or less marked pes cavus. The deformity will be more marked in young people since the forces producing it act upon less rigid skeletal structures and during a period of growth, than in old people where the structures are more rigid.

(The physiological basis of the muscle tone and of rigidity is probably far more complicated than stated above, but the explanation given, so far as it goes, quite suffices for the case at issue.)

As a strong argument in favour of the truth of this explanation of pes cavus the three exceptional cases of hemiplegia with a flexor response upon the affected side may be again mentioned. The deformity of the affected foot in these cases resembled the position a normal foot assumes at the height of a vigorous flexor response, just as pes cavus resembles the position of a foot at the height of an extensor response.

Conclusions.

(1) This investigation has confirmed those of Babinski, Van Gehuchten and Brissaud in all essential points.

(2) The plantar reflex of healthy subjects, with the exception of infants, consists of a regular succession of contraction in certain muscles to increasing stimuli. The response may be confined to certain muscles of the hip. It

is doubtful whether the plantar reflex is ever constantly and completely absent in healthy subjects. The term "flexor response" is proposed for this form of plantar reflex.

(3) In infants, up till the age of learning to walk, the succession of the contraction of the muscles in the plantar reflex is entirely different from that seen in the adult; the change from the one form of the plantar reflex to the other occurring gradually with the establishment of complete volitional control over the legs, usually between the second and third year of life. The term "infantile response" is proposed for this form of plantar reflex.

(4) During sleep the plantar reflexes are diminished, and the infantile and adult forms preserved, except in some children up to the age of 12 years, where in deep sleep the infantile form of reflex returns.

(5) In almost all cases of lesions of the pyramidal systems the form of plantar reflex is changed, a plantar reflex resembling closely that found in infants appearing. This change in the form of the reflex is one of the first signs of such lesions to appear, and is the last to disappear when the lesion is temporary. It may be the only unequivocal objective sign of a lesion of the pyramidal system. This form of reflex is never found under other conditions, and is a sign of great clinical value. The term "extensor response" is proposed for this form of the plantar reflex.

(6) In cases of total transverse lesion of the cord, the extensor response is the only reflex phenomenon present in the lower limbs.

(7) In functional cases the plantar reflex is often difficult to elicit, and there is frequently no response in the foot, but in such cases a response may usually be observed in the hip muscles. The form of reflex is the flexor response.

(8) In tabes dorsalis the plantar reflex was entirely absent in 20 per cent. of the cases. The response is often confined to the hip muscles. The attempt to obtain the reflex frequently may set up irregular movements of the foot lasting some time. The reflex when present is the flexor response.

(9) In peripheral neuritis the reflex when present is the flexor response. The hip muscles respond alone in some cases.

(10) In cerebral and cerebellar tumours the flexor response occurs if there be no involvement of the pyramidal system.

(11) In neurasthenia, chorea, paralysis agitans, poliomyelitis, myopathy and sciatica the flexor response is found.

(12) In lesions of the pyramidal system a degree of pes cavus is frequently found. It is intimately associated with the extensor response in the plantar reflex, and is produced by a state of reflex hypertonicity preponderating in those muscles which respond most vigorously in the plantar reflex. In all such cases of pes cavus evidence of increased tone in certain muscles can be demonstrated.

(13) The theory that the pes cavus of spastic conditions is due to weakness of the interossei is not justified.

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NOTES ON THE CHROMOPHILIC MATERIAL IN THE MOTOR CELLS OF BRAIN AND CORD, NORMAL (ANIMAL) AND PATHOLOGICAL (HUMAN), AND ON THE REACTION (ACID OR ALKALINE) OF THE CORTEX AND CEREBRO-SPINAL FLUID.

BY JOHN TURNER, M.B.ABERD.

I.

SINCE the publication in BRAIN (Winter, 1897) of a method of examining fresh cells, I have, at the suggestion of Dr. Mott, used a solution of methylene blue in normal salt.

With this the anterior cornual cells of the cow, pig, rat, rabbit and rook have been examined, as before described, as soon after killing as the cord could be extracted. In every case, even when no other medium (Farrant's solution) has been employed, and the stained little piece merely pressed out in its own moisture under a cover glass, the chromophilic elements have been distinctly visible in their usual form and arrangement.

And as regards human cortex no difference can be detected whether one uses a solution of methylene blue in water or in normal salt; and this refers to material which, in some cases, was examined only a few hours after death (from one to four or five hours).

These observations are in opposition to Held's view, that the form the chromophilic elements (Nissl bodies) assume is artificially produced by fixing reagents, but do not affect his further supposition that the acidity of the cortex set up after death, may precipitate the granules of the hyaloplasm in the form of Nissl bodies. Van Lenhossek has seen in spinal ganglia cells brought under the microscope directly after death without any addition of reagents, the grains of the cell protoplasm.[1]

But although it may be shown that the Nissl bodies exist in quite fresh cells after death, there remains the possibility that they are precipitated as such by an acid reaction in the cortex, due to *post-mortem* changes. Held asserts that the Nissl bodies are insoluble in weak and concentrated mineral acids, but easily soluble in weak and concentrated alkalies, and he contends that during life the alkaline nature of the nerve cell fluid holds these bodies in solution, but that after death an acid reaction is set up by which a precipitation of granules takes place in the form of Nissl bodies.

There is a fact furnished by pathology and which will be further referred to later on, also opposed to this theory of Held's, and that is, that in certain morbid conditions, the bulky chromophilic spindles and blocks usually met with in healthy cells, dwindle away until they become the finest imaginable threads before disappearing altogether. The observation previously made that chromophilic material is met with in the fore-horn cells of animals freshly killed, does not prove anything decisively against the idea that the Nissl bodies are precipitated as granules from a fluid hyaloplasm that has become acid, because, however shortly after killing we test the nervous substance, we obtain both an acid and an alkaline reaction by using different indicators. This I have done with animals immediately after killing, and with human beings as short a time as seventy minutes after death, and the results of these experiments are given below.

Halliburton[2] states that he has never failed to find an alkaline reaction in fresh brain, cord or nerve, becoming, however, as a rule, rapidly acid after death. Langendorff (quoted by Halliburton) experimenting with frogs, rabbits and guinea-pigs, finds the central nervous system to be alkaline during life, rapidly becoming acid after exposure or death.

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[1] Quoted by Goldschieder and Flatau. *Norm. und Path. anat. der Nerven zellen*, p. 14.

[2] Text book of Chem. Physiol. and Pathol., p. 515.

Heidenhain and Gschleidlen state that the grey matter of the brain is acid even during life, probably due, they think, to lactic acid. J. Moleschott and A. Battistini, using phenolphthalein, found that the brain and spinal cord were acid, the grey more than the white.

With the exception of the last, no mention is made in Halliburton of the indicator used.

I have tested the reaction of the cortex and cerebro-spinal fluid in thirty-seven bodies of insane patients varying from one to forty-four hours after death, and using phenolphthalein, litmus, and methyl orange as indicators, and the grey matter (generally of spinal cord) of five animals (rook, rat, rabbit, pig, cow).

The results are always the same for the human cortex and cerebro-spinal fluid.

Phenolphthalein.—In all cases (twenty-seven human, and five animals) the grey matter discharged the pink colour from an alkaline (KHO) solution of the indicator.

The cerebro-spinal fluid of the human brains also *invariably* gave an acid reaction.

Litmus.—The paper was used; and when care was taken to avoid contaminating it by the cerebro-spinal fluid, the results were likewise constant.

In twenty-eight human brains the cortex was always acid.

Of the five animals, the rook's grey matter, tested one hour and forty minutes after killing, gave an acid. In the other four, tested as soon as the cord (or brain) could be extracted after killing, an amphoteric reaction was obtained, but the alkaline seemed the stronger, for when the blue paper was applied it turned faintly red; but this colour was evanescent, and faded after removal of the paper, but with red paper a permanent and decided blue was obtained.

With the cerebro-spinal fluid tested in thirty human brains, varying from seventy minutes to forty-four hours after death, there was also an amphoteric reaction in twenty-nine of the cases, for the blue paper was faintly tinged red, but the colour quickly faded, whilst the red paper was somewhat slowly turned of a decided and permanent blue. In one case, five and a half hours after death, only an acid reaction was obtained.

Methyl orange.—This indicator, although it is not sensitive to most organic acids, reacts to lactic acid, yet, curiously enough, it only gives an alkaline reaction with cerebro-spinal fluid which after death contains this acid.

I have never obtained any reactions with yellow (alkaline) solutions, but with ten human brains and one cow's, the former varying from two and a half to twenty hours after death, a decided alkaline reaction always resulted.

With the cerebro-spinal fluid of sixteen cases also an alkaline reaction resulted in every one.

It will be seen from the foregoing that in one particular only does the reaction of the cortex differ from that of the cerebro-spinal fluid, in that the former is acid to litmus, the latter alkaline. Naturally the cerebro-spinal fluid, which permeates the cortex in all directions, will to a large extent determine its reaction; but the immediate and decided reddening of blue litmus paper shows that the grey matter contains substances not present in the cerebro-spinal fluid, or, if present, not in sufficient amount to influence its behaviour to litmus.

Lactic acid was tested for by carbol. ferric chloride (4 per cent. carbolic acid 10 c.c., water 20 c.c., liq. ferri perchlor. B.P. one drop) in sixteen cases.

A roughly quantitative estimation was attempted by always using 5 c.c. of the purple solution and counting the number of drops required to turn it completely yellow. This varied from seven to thirty, and, generally speaking, the number of drops was smaller the longer time which had elapsed after death when the fluid was tested, but not invariably. In three cases where the cerebro-spinal fluid taken from bodies seventy minutes, two and a half and twelve hours after death respectively was tested at the time of the autopsy and then allowed to stand for forty-eight hours, no very marked difference was found in the amount of lactic acid at these two different times, but if any reliance is to be placed on the quantitative method employed, it indicated a slight diminution in the amount of lactic acid on standing.

Now, although lactic acid is found in the cerebro-spinal fluid as shortly as seventy minutes after death, it does not appear to be present in the fluid during life, nor to be formed in it after removal during life.

I have not directly tested for it under these circumstances, but from the fact that a sample removed by lumbar puncture in the case of a male general paralytic gave an *alkaline* reaction to phenolphthalein (which is sensitive to organic acids), I think it is highly probable that in this case lactic acid was not present. This same fluid, after standing forty-four and a half hours, still gave a distinctly alkaline reaction to phenolphthalein.

The above-mentioned observation tends to show that the lactic acid formed in the cerebro-spinal fluid after death is a *post-mortem* product, and that it is formed by chemical change taking place (*post-mortem*) in the brain; from whence it is carried to the fluid which bathes all parts of the brain.

I would note here that although with a freshly-killed cow a lactic acid reaction was slowly obtained from a piece of cortex in carbol. ferric chloride, yet this can quite readily be accounted for on the assumption that the protoplasm was killed by the reagent and produced the lactic acid in consequence there and then.

The results of these observations show that in human brains and animal both acid and alkaline substances are present in the cortex and cerebro-spinal fluid.

Certain German observers have already stated that such was the case, for Liebreich and Langendorff, using fresh pieces of cortex, found that they turned litmus blue, whilst Liebarkühn and Edinger, using an infusion of alizarin, got an acid reaction.

SUMMARY.

(1) Chromophilic material in the form of Nissl bodies is met with in animals immediately after killing and in human

beings at least seventy minutes after death, when the nervous substance has merely been coloured by a solution of methylene blue in normal salt without any further addition of reagents.

(2) The fact that in some forms of diseased nerve cells the Nissl bodies show a gradual attenuation so that they dwindle down from bulky spindles and blocks to the finest imaginable threads, is opposed to the idea that they are produced by a precipitation after death.

(3) The reaction of the cortex varies with different indicators, showing that it contains both acid and alkaline substances.

(4) Its variations are constant, whether tested two hours or forty-four hours after death, and are as follows:—acid to phenolphthalein and litmus, alkaline to methyl orange.

(5) With animals killed and immediately tested, the grey matter gave similar reactions with phenolphthalein and methyl orange, but was alkaline to litmus.

(6) The reactions of the cerebro-spinal fluid differ from the cortex, in that with litmus an alkaline reaction is obtained. Otherwise they are the same. These results do not differ, whether the fluid is tested seventy minutes or forty-four hours after death.

(7) Lactic acid is present always in cerebro-spinal fluid after death, and appears to increase with the length of the interval which has elapsed between the time of death and the time of testing.

II.

Goldscheider and Flatau,[1] by subjecting rabbits to a high temperature in a thermostat, succeeded in producing a condition of pyrexia in these animals associated with a change in the fore-horn motor cells of the spinal cord. These changes were as follows:—

The cells appeared larger than normal, and stained (by Nissl's method) of a pale blue colour, opaque and homogeneous; a finely granular condition could be discerned in relation with an ill-defined network of threads. Here and there were dark specks, probably the remains of Nissl bodies.

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[1] *Normale und path. Anat. der Nervenzellen.*

The nucleus was either not visible or indistinct, it stained homogeneously, and was sprinkled with the finest granules, and was not sharply outlined, and generally, as in the normal condition it was paler than the cell body.

The nucleolus was generally irregular, jagged, and darkly stained.

The dendrites were very pale and swollen, and presented slight varicosities; they showed no spindles, but only ill-defined granules.

As a result of numerous experiments, they came to the conclusion that a well-marked change of the above description was found as soon as the animal's temperature (which ranges normally from 101° to 102·7° F.) rose above 109·4°, and that if one allows the rise of temperature to last about three hours from 107·3° to 107·6°, then the first signs of alteration were visible on the periphery of individual cells.

Further, that a restitution from this condition occurred if the animal was allowed to recover; that it began after twenty-five and a half hours and was complete in sixty-eight hours.

Moxter, experimenting in somewhat different ways with artificially raised temperature in rabbits, obtained practically the same results as Goldscheider and Flatau, and he concluded that—

(1) A change in the forehorn cells is found after twenty-two and a half hours under the influence of a temperature between 104·9° and 106·7°.

(2) After several days' intermittent temperature between 100·4° and 106·3° no changes were found.

(3) Twenty-three hours, with a temperature varying from 102·5° to 105·2°, no changes were found, not even where the heightened temperature was several times renewed.

(4) That even in rabbits with lower temperatures than

those produced in the experiments an almost complete chromatolysis was met with, if the lower temperature was allowed to act sufficiently long.

Goldscheider and Flatau quote two cases where with pyrexia similar changes were found in the fore-horn cells of the cord. In the first—a man suffering from tetanus, whose temperature for the four days prior to death ranged from 98·6° to 101·1°, rising on the evening of death to 103·8°. The changes were found in all heights of the cord, in the cells both of fore and hind-horn, in the middle zone, and in Clarke's column. In the second—a girl with scarlet fever whose temperature for the last twelve hours varied between 104·9° and 105·6°—the cells of the cervical region were more affected than those of the lumbar.

Dejerine (quoted by Goldscheider and Flatau) found also in a case of pneumonia a decided chromatolysis of the nerve-cells of the spinal cord, which he considers similar to those seen in artificial pyrexia in rabbits.

Lugaro[1] asserts that experimental pyrexia causes complete disintegration of the chromatic part of the protoplasm of cortical and other nerve-cells without producing any other very marked change.

In a paper read before the Med. Psych. Soc. in May, 1898, I mentioned five cases of insanity in which I found changes in the motor cortex evidently very similar to those described (and figured) by Goldscheider and Flatau. At that time I was unaware of these experiments, yet the idea that they might have been caused by pyrexia had entered my mind, but had been dismissed because in other cases I had examined, where as high or higher temperatures had existed for some time before death, no such changes were found, and also because similar changes were occasionally met with in cases in which at least several days prior to death the temperature had not been raised.

Yet another reason against the view that these alterations were due solely to pyrexia was that in several cases where the altered cells were found in the cortex those of the fore-horn, cervical spinal cord, and hypoglossal nuclei showed a fairly normal arrangement and amount of chromophilic material.

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[1] Quoted by Robertson and Orr. *Jour. Mental Science*, October, 1898, p. 740.

Whilst I think that such reasons forbid us to regard pyrexia as the essential cause of the changes I described, it seems highly probable, considering how often pyrexia is associated with them, that such a condition will lead to alterations in the metabolism capable under favourable circumstances of producing these changes in the nerve-cells.

It is my intention here to consider in more detail the condition previously described, and to bring forward other examples since met with, because this condition seems to be of a very interesting nature, and also because others[1] have assumed that it was merely the accompaniment of pyrexia.

I do not for one moment wish it to be considered that it is peculiar to insanity—such is not the case; amongst the number now brought together is a case of typhoid fever in a female, whose brain showed the changed cells, and although she was not of normal intellect, her mental condition was such as to render it in the highest degree unlikely that the changes found in her nerve-cells were due to insanity, but that they were consequent on the typhoid fever.

Before proceeding to a description of the so-called pyrexial cell, a list is appended of cases in which there was a high temperature up to death and in which no trace of a single cell having any likeness to those in question was to be seen either in freshly squeezed-out films or in sections. A larger number of cases might have been brought together very easily, but I have restricted myself to those in which the temperature was ascertained to be high till at least a few hours before death so as to exclude the possible objection that restitution changes had taken place, and also to such cases in which beyond a certain amount of chromatolysis no very obvious alterations were noted in the cells when examined by the fresh method.

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[1] Robertson and Orr. *Jour. of Mental Science*, October, 1898.

TABLE I.

No.	Sex.	Form of Insanity.	Age.	Cause of death.	Temperature in axilla (F.).
1	F.	Demented ..	38	Pneumonia	For two days prior to death varied between 101·2° and 102·8°, gradually rose till it reached 106° ten minutes before death
2	F.	Always weak-minded; maniacal	62	Abscess and necrosis of bone	For five days before death was always above 101°. (Highest = 103·8°.) On the morning of her death = 102°
3	F.	Chronic mania ..	48	Erysipelas ..	On the day before death it was 102° in the morning, 104° in evening. Not taken previously
4	F.	Puerperal mania	29	Pleurisy and Pneumonia	For the last few days as follows:—E., 106°; M., 103·8°; E., 105·2°; M., 103·6°; E., 105°; M., 103°.
5	F.	Acute mania ..	24	Pneumonia and Phthisis	For the last few days as follows: — M., 100°; 101·4°; 101·2°; 101·6°. E., 101·6°; 102°; 102·5°; 105°
6	M.	Idiot	7	Pneumonia and status epilepticus	The day before death as follows:—M., 105°; E., 103°. The next day it was 102·8° at 4 p.m., and he died at 9.25 p.m.
7	F.	Weak-minded; epileptic	27	Phthisis ..	For the last three days as follows: — M., 100°; 100·4°; 103·6°. E., 104·2°; 104·6°; 103°; falling to 101·6° at time of death.

If pyrexia alone could account for the change in cells under discussion, it is quite inexplicable why in such a case as No. 4, where for four days prior to death the temperature had stood at from 5° to 8° above normal, no such change was found.

Portions from the top of the ascending frontal of each of these cases were examined both in the fresh condition and after hardening.

(*A*) In the fresh cells merely coloured with methylene blue no very marked departure from the normal as regards the arrangement and quantity of chromophilic material could be determined.

In some the centre had a somewhat paler and washed-out appearance, whilst others showed granular degeneration of the Nissl bodies, but such were in a decided minority.

The cell bodies were generally irregularly angular, with many processes and not so large as in the so-called pyrexial cell, and the dendrites appeared normal in all respects, never showing the dull, pale blue uniform staining nor the very marked fragility found in such cells.

There were no special features which need be noted in regard to the nucleus. In some cases the nucleolus was large (12 μ) and pale, in others of normal size and dark. In others it had quite disappeared.

(*B*) In the portions of the ascending frontal which were fixed either in alcohol or sublimate, infiltrated with paraffin, and stained either with methylene blue, thionin or toluidine blue, there was a great uniformity in the appearance of the cells as regards the condition of the Nissl bodies (see figs. 1, 2, and 5).

Whilst many presented a fairly normal appearance, in the majority a very marked chromatolysis was found in all but one (No. 5) of the cases. Its characters were as follows:—

The apex, dendrites, and periphery of cell body always contained large, darkly-stained spindles, threads, or blocks.

The interior of the cell body is occupied by a paler and more uniformly stained substance, which resolves itself into a collection of pale and darker granules when highly magnified.

What I wish to draw attention to is the fact that although there is a considerable disappearance of chromophilic material in the cell, that which remains has not the appearance seen in the so-called pyrexial cell. There is no attenuation of the Nissl bodies; those which remain are as bulky and as deeply stained as usual. The condition of chromatolysis met with is quite unlike that obtained either in the partial disappearance of the Nissl bodies with pyrexia or their partial restitution with the subsidence of the pyrexia.

Except in one case (No. 7) there was no appearance of any undue shrinking of the cells, and their ground substance is nearly colourless.

The apex and dendrites are stout and have a regular outline presenting no varicosities. The nucleus is round or oval, generally with a distinct limiting boundary line, and more or less filled with a pale, amorphous material.

The nucleolus is generally darkly stained and regular in outline and varies from 4 to 6 μ in diameter. Often pale spaces or even vacuoles are seen in it.

Besides the ascending frontal in case No. 1 the frontal and occipital cortex regions were also examined, and in case No. 7 the cervical and lumbar enlargements of the cord and the hypoglossal nuclei. In the former case the pyramidal cells of the frontal region tallied with those of the ascending frontal, and a photograph of one of them is given in BRAIN (see Winter number, 1897, p. 450, fig. 1), which shows the large amount of chromophilic material and its arrangement. Similarly the giant-cells of the occipital cortex showed no marked deviations from the normal.

In case No. 7 both fresh and hardened specimens of cord were examined.

In fresh preparations of the hypoglossal nuclei the cells showed a perfectly normal appearance in the arrangement, &c., of the Nissl bodies. In the lumbar enlargement the motor cells of the fore-horn were fragile; the body of the cell was occupied by a mass of rather large granules of chromatin (granular degeneration). The dendrites appeared normal.

In sections.—Many of the fore-horn cells of the cervical enlargement presented considerable chromatolysis, characterised by the same features as mentioned in describing the ascending frontal cells, others appeared normal. In the lumbar enlargement a similar appearance of cells was seen as in the fresh preparations, the cell is filled with masses of chromatin rather smaller than usual and not rod-shaped (crumbling of chromophilic material). At the boundary the masses are larger and of a square contour. The dendrites appear normal.

Turning now to the cases which showed a similar condition of cells to that found in rabbits' cords after experimental pyrexia, the following table contains a list of these, and gives the form of insanity and the cause of death, &c.

TABLE II.

No	Sex.	Age.	Form of Insanity.	Cause of death.	Remarks.
1	M.	40	Acute general paralysis	Pneumonia ..	Recently had a seizure before his death. Temperature not stated
2	M.	49	General paralysis	Seizure ..	His temperature rose to 105° F. before death
3	F.	35	Weak-minded from epilepsy	Status epilepticus; pneumonia	Temp. for last three days: M., 100°; 100·4°; 101°. E., 101·4°; 100·4°. Died 9.20 p.m.
4	F.	25	Acute puerperal mania	Peritonitis ..	Temp. at 6 p.m. of day of admission was 100·4°; next morning, 100·2°; 7 p.m., 103·4°; 9.15 p.m., 104·6°; 11.45 p.m., died
5	F.	49	General paralysis	Seizure ..	Temp. on morning of death = 103°
6	F.	58	Dementia and epileptic	Status epilepticus	Two days before death, evening temp., 99·4°; next morning, 98·4°; at 6 p.m., 106·6°. Died 7.30 a.m. next day
7	F.	24	Acute delirious mania	—	Temp. not raised for several days prior to death
8	M.	39	General paralysis (chronic lead poisoning)	General paralysis	Temp. not stated
9	F.	44	Weak-minded and fatuous; result of chronic alcoholism	Typhoid fever	Temp. high
10	F.	48	Chronic mania ..	Pneumonia and pericarditis	Had a temp. ranging between 102° and 104° for nine days prior to death
11	F.	40	Dementia ..	Cerebral tumour (gliosarcoma)	Temp. always subnormal.

Although in most there was a raised temperature immediately prior to death, yet there are two exceptions to this rule (Nos. 7 and 11), and in one other case (No. 3) it can scarcely be supposed that the temperature reached was sufficient, on Goldscheider and Flatau's showing, to have caused the changes in the cells which were met with.

Portions of brain, as in the last series, were taken from the top of the ascending frontal and examined both in a fresh state and after hardening.

(*A*) Fresh films stained in methylene blue.

Although the following description refers more particularly to the giant-cells of the cortex, yet it also applies to the other pyramidal cells. The cells appear large and blown out; they have to a large extent lost their multi-angular shape and have a more rounded contour. The cell body and apex stains of a dull, uniform blue, but with high magnification a finely granular condition is seen. Very often towards and in the apex are seen thin threads stained of a darker blue, which are the attenuated remains of Nissl bodies (fig. 7).

Although generally not much pigment is present, sometimes there is a large amount of it.

The dendrites, which are fairly numerous and fairly bulky, stain throughout of the same dull blue tint as the cell body. They are extremely fragile. The nucleus, when visible, is most often a pale, ill-defined zone around the nucleolus.

The nucleolus is generally central, and is very rarely displaced to the side of the cell. It is always round or oval, but varies considerably in size (from 5 to 12 μ) and depth of staining. To a large extent the latter is in inverse proportion to its size; the larger it gets the paler it becomes, until in some cells it is quite invisible.

In cases 2, 7, 9, and 10 it is in almost all cells very pale and large (11 μ), with a blurred outline. In some cells it is only just visible, in others quite invisible.

In cases 3, 5, and 6 it is generally small (5 to 6 μ), very dark—indeed, almost black—and stands out prominently from the pale background of the cell body.

In the other cases there is a more general mixture of the two kinds described, so that it is difficult to say whether the large pale or the small dark nucleolus predominates.

The large pale nucleolus in sections from hardened tissue shows often as pale multi-loculated bodies not much larger than usual, the probability being that by dehydration they have shrunk.

Vacuolation or irregular staining of the nucleolus is not seen in fresh preparations before fixing.

With the exception of the differences noted in the nucleoli there is a great likeness between the cells of all the cases. My description will apply to the great majority of the cells seen, but some are met with which are very pale and appear as ghost-like forms of the others. In some of these pale cells a nucleus is seen staining of much the same depth as the cell body, with a definite but fine border.

(*B*) On examining sections which have been subjected to fixing agents (alcohol or sublimate) the cells no longer present in the different cases quite such an uniform character, but the difference is mainly in the shape and depth of staining.

The giant-cells are generally large and rounded, filling out the entire pericellular space, but with some cells there appears to have been considerable shrinking, and this space is large.

The dendrites are manifestly thinner than in healthy cells, and probably less numerous, and not infrequently show varicose dilatations.

Sections stained in thionin or toluidin blue present a very characteristic appearance, owing to the universal but pale violet-tinted staining of the cell and its processes. The whole of the protoplasm staining of the same depth. It appears impossible with these stains to get a deep colour in the cells. High magnification of the apparently uniform cell body shows a delicately granular background, with larger and darker granules sprinkled about. In many cells remains of Nissl bodies can be detected in the apex and about the periphery. These are in the form of delicate threads (figs. 3, 4, 10, and 11).

This gradual attenuation of the Nissl bodies, until the originally big spindles or rods have dwindled away to fine threads, is a point worthy of note in reference to the question as to the origin of these bodies by precipitation, and cannot easily be accounted for by Held's theory.

In the sections a large cell is occasionally seen which has absorbed the stain deeply, and appears blotchy, showing little or no detail, but these are in most cases very few and far between.

The nucleus presents no peculiarities from those described before; we see an ill-defined granular mass arranged more or less in the form of an irregular mesh work, and described as such by German observers, but which it seems more likely is merely the representation of a coagulated albuminous mass, which during life and before fixing occupied this body as a fluid or semi-fluid material.

The nucleolus varies somewhat, corresponding probably to the variations noted in the films. It often, although darkly stained, shows a number of pale or colourless spots (fig. 4). In other cases it is pale and with a multiloculated appearance.

There is not the extreme difference in size met with in the fresh preparations, probably because the large pale nucleoli noted in the latter are more fluid in nature and have contracted more when subjected to dehydrating agents.

In cases 7, 10, and 11, besides the ascending frontal, other parts of the nervous system were examined, viz., the cervical cord in No. 7 and cervical cord and hypoglossal nuclei in Nos. 10 and 11.

In these parts, both in fresh and hardened preparations, the chromophilic material appeared generally in normal amount and arrangement, but in some few cells chromatolysis of the character previously noted was seen.

There can be no question that as far as morphological appearances go the cells of all the cases, with the exception perhaps of one (No. 7), represent a similar pathological condition, and as regards this one there are certain facts which render it probable that it belongs to the same category, but probably in a more advanced state of disease.

In fresh preparations its cells appeared identical with those of the other cases, and in certain parts of the sections, always at the base of a convolution, some were seen which were not shrunken and appeared identical to those seen in sections from the other cases, also in nearly all the sections from these latter certain cells were met with which stained densely and appeared shrunken, and, in fact, had very much the appearance of the majority seen in No. 7.

Case No. 7 appears of sufficient interest to warrant a brief description. It was that of a well-developed, strong girl, aged 21, who, previously to her mental affection, had always had good health. She was admitted here suffering from acute delirious mania of only a few days' duration, and whilst in this state had jumped out of a bedroom window and badly bruised herself, but beyond the bruises did not appear to have sustained any serious injury to her system.

She was violently excited for the first few days after admission, and then showed signs of collapse with intervals of restlessness, when she would toss her arms about and move her head. A large bleb formed on her right heel, her tongue, which at first had been heavily furred but moist, became dry, brown, and cracked, and she died seven days after admission. Her temperature and pulse was as follows: —August 2, 5.30 p.m., 101·4°; pulse 123. August 4, 4 p.m., 97·8°. August 5, 6.45 p.m., 99·8°; pulse 142. August 6, 9 a.m., 98·6°; pulse 123; 7 p.m., 99·2°. August 7, 7.30 a.m., 98·6°; pulse 124; 7 p.m., 98·6°. August 8, 8.30 a.m., 98·6°; 6 p.m., 98·4°. August 9, 8.30 a.m., 98·4°; 7.30 p.m., 98·2°. She died at 6.20 a.m. on the 10th. The autopsy was held four and a half hours after death.

On the external surface of the dura mater was a thin, soft, dark clot, 40 × 30 mm.; it lay over the middle portion of the right second frontal convolution. The veins of the arachnoid were much engorged. There was excess of pale, reddish fluid in the lateral ventricles. No other morbid appearances noted in the head except perhaps some shrinking of the convolutions at the vertex, and the cortex was dark in colour on section. The encephalon weighed 1,218 grammes. The heart was small (245 grammes), and there were some atheromatous patches on the aorta near the valves. The liver was pale. In other respects the thoracic and abdominal viscera appeared healthy. Portions of the ascending frontal at the top on both sides were examined fresh, other pieces from the same region were fixed in 10 per cent. formal. followed by absolute alcohol. Pieces of the liver and kidneys were put into Müller, and when examined microscopically the latter, except for very slight fatty degeneration in the superficial parts of the cortex, appeared fairly normal, but the liver showed very general and marked fine, fatty degeneration at the centre of the lobules.

In the brain the fresh films showed the giant-cells of the motor cortex, quite indistinguishable from those already described in general appearance and with the same extremely fragile dendrites. Fig. 7 shows one of them. There is evidence of remains of Nissl bodies in the form of fine threads in the apex.

The nucleolus is large, pale, and indistinct. The dendrites stain of a pale, dull blue, and all over alike.

The only difference noted in the cells was that some were pale and ghost-like, others darker and more dense.

In the sections the nerve-cells of the second layer appeared normal, but in all the deeper layers they were much altered. The pyramidal cells staining uniformly throughout of a somewhat paler colour than usual and with absolutely no chromophilic material, presented identically the same appearance as the pyramidal cells seen in the other cases of Table II.

The greater number of the large nerve-cells (giants) were much shrunken, darkly stained, and somewhat distorted, with a wide pericellular space around them. The staining of the cell body was so dense and diffuse that all detail was obscured (see figs. 6 and 8).

The nucleus was generally central and round or oval, but sometimes irregularly encroached upon by the protoplasm of the cell body. Nucleolus, round and dark. The dendrites, few in number, were dark and thin and devoid of chromophilic material, showing in places varicose dilatations along their course. The apex was very irregular in contour and in the way it stained, being very dark in some places, pale in others.

Others of the big nerve-cells were less darkly stained, and appeared as though consisting of fibres arranged as an irregular meshwork, whilst the apex had a rough, unravelled aspect (fig. 9). And lastly, as before mentioned, a few cells characteristic of the other cases of Table II. were seen.

The blood-vessels were tortuous and showed masses of pigment, staining of a green colour, lying in the adventitia and perivascular spaces. In some of the larger vessels in the pia there was an aggregation of numbers of polymorphonuclear leucocytes filling up their lumen, whilst others were wholely or partially blocked up by a homogeneous hyaline material which stained of a greenish blue.

No appearance of any neuroglia proliferation.

The upper part of the cervical cord was also examined. The fore-horn cells were shrunken and deeply stained; the majority show the usual arrangement and quantity of Nissl bodies, whilst others with their dendrites are throughout stained darkly.

Now, unless we suppose that the fall, which probably was the cause of the small hæmorrhage on the dura, also produced such disturbance in the cerebral hemispheres as to give rise to the condition of cells found—a supposition not very probable—then we must take it that the pathological appearances noted were directly associated with the insanity.

What relation did the one bear to the other?

I would suggest from the following considerations:—

(1) The acute nature of the mania and its rapidly fatal result,

(2) The absence of naked eye lesions to account for such a termination,

(3) The changes in the nerve-cells, and

(4) The highly suggestive fact of the fatty degeneration of the liver in so young a girl.

That a wide-spread toxic influence was at work and that the chain of events was somewhat as follows:—

(1) Mental disturbance.

(2) Perverted metabolism resulting in the setting free of toxins in the system.

(3) Action of these on already disordered nervous system. This also is the hypothesis that I would advance to account for the changes in the cells of the other nine cases.

A glance at the cause of death in Table II. will at least show that the circumstances under which we come across such cells are highly suggestive of poisoning, and to give an instance illustrating this we can almost count upon meeting with them in the brains of general paralytics who have died in seizures.

But whether this explanation is accepted or not, I think that sufficient reasons have been brought forward to show that the changes under consideration are not due directly or solely to pyrexia.

SUMMARY (PART II.).

Nerve-cells are met with in the human cortex, which are similar in appearance to the fore-horn cells found in the cords of rabbits after experimental pyrexia, but that pyrexia alone cannot account for their condition is shown by the following facts:—

(*a*) The frequent occurrence of pyrexia lasting until death in cases where such cells are not found, either in brain, hypoglossal nuclei, or cord.

(*b*) The occurrence of these cells in the cortex of cases which had shown no pyrexia, or in which the pyrexia had been too slight to account for them.

(*c*) And finally, the fact that in certain cases, while these cells were found in the cortex they were not met with in the hypoglossal nuclei or in the cervical cord, the nerve-cells in these places showing the presence of Nissl bodies in a fairly normal condition.

NOTE.

Since the above was written I have examined the brain from a man, age 34, suffering from acute mania, who died of diphtheria. His temperature two days before he died was 102° F., and although I have no record of it before that time, there can be no reasonable doubt that it was high for some days previously, as when it was first taken the disease was in an advanced stage and his neck glands much involved. The day following it had risen considerably, and shortly before his death was 104° F.

Portions of the ascending frontal convolutions of both sides were examined fresh and after fixing in sublimate.

As regards the fresh method, although some eight or nine films were prepared and numbers of large nerve-cells seen in all, not one showed any appearance of the so-called pyrexial cell.

A very considerable number was stained of a dark, bright blue and had a normal stichochrome arrangement of their chromophilic elements throughout the entire cell; the dendrites were bulky and unstained, except for distinct threads of chromophilic material.

The majority, whilst presenting a similar appearance to the above in apex, dendrites, and periphery of cell body, showed in the interior a condition of granular degeneration of the Nissl bodies.

In some the granules are big and close set (dark cells), in others smaller and further apart (pale cells).

A perfectly analagous appearance of big cells was seen in the sections; and, in respect to the smaller pyramidal cells, although the chromophilic material may have been diminished, yet they failed entirely to show the quite characteristic appearances described before in the cases associated with the so-called pyrexial cells.

In many of the big cells in the films the nucleolus was pale, ill-defined, and more or less increased in size, in others it was quite invisible; but in the sections all of those seen were dark, sharply defined, and not above their usual size.

That there is some relation between certain fevers and states of insanity has long been recognised, and it is interesting to note that manifest changes of the nerve-cells can be detected in two of those fevers after attacks of which improvement or recovery of mental condition has occurred. I refer to the typhoid fever case recorded above and to a case of scarlet fever mentioned by Goldscheider and Flatau. In this case, however, only the changed condition of the motor cells of the spinal cord is referred to, and apparently the brain was not examined.

As far as I know no such improvement has been noted in cases of insanity after attacks of diphtheria, which does not appear to affect the central nerve-cells so profoundly or in which at least there is not the very palpable alteration such as are seen with typhoid and scarlet fever.

DESCRIPTION OF THE FIGURES.

All were photographed with $\frac{1}{12}$ oil immersion (Beck), No. 2 eye-piece (=$\frac{290}{1}$), with the exception of No. 7, which is with $\frac{1}{8}$ in. This last is from a fresh preparation, the others from sections.

FIG. 1.

Shows a fairly normal arrangement of Nissl bodies in the form of blocks and granules; the axis cylinder is also seen, and one stout dentrite with chromophilic threads in it (Case 5, Table I.).

FIG. 2.

Two cells from same case with normal arrangement of Nissl bodies. At the lower left hand part of the right cell is the axis cylinder eminence. Some pigment at the lower end of left cell.

FIG. 3.

Two cells from Case 10, Table II. Both stain diffusely and rather deeply, and show coarser granules on a finer granular background. In the upper cell a few attenuated threads of chromalin are seen in the apex. Small vacuoles in nucleolus.

FIG. 4.

Paler cell from same case with pigment at lower end. The attenuated chromophilic threads are well shown. Nucleolus vacuolated.

FIG. 5.

Cell from Case 3, Table I. Pigment in lower end. Bulky chromophilic spindles in upper part. Nucleolus vacuolated. A stout dendrite shown, unstained except for the chromophilic threads.

FIG. 6.

A darkly stained cell from Case 7, Table II., showing no chromophilic material. Apex and dendrites darkly stained throughout; the latter thin, and with varicose dilatation.

FIG. 7.

Same case. A fresh cell with a small patch of pigment at lower right end. Faint remains of chromophilic material seen in apex. Dendrites stain uniformly and are devoid of chromophilic material. Nucleolus ill-defined.

FIG. 8.

Same case. Darkly stained cell, showing a very ragged and irregularly contoured apex.

FIG. 9.

Same case. Pale cell with rough, irregular mesh work appearance of body and apex.

FIGS. 10, 11, 12.

Cells from a case of typhoid fever, Case 9, Table II.

Fig. 10 is a rather darkly stained cell with thin threads of chromophilic material shown in the apex end processes. Nucleolus is vacuolated. Fig. 11 also shows fine threads in apex and upper two-thirds of body; the lower third is occupied by pigment. Fig. 12 is a very pale cell, uniformly stained, except for one or two little masses of chromophilic material. Nucleolus is vacuolated.

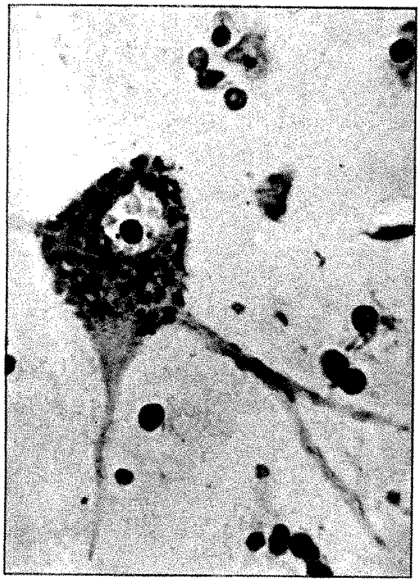

FIG. 1.

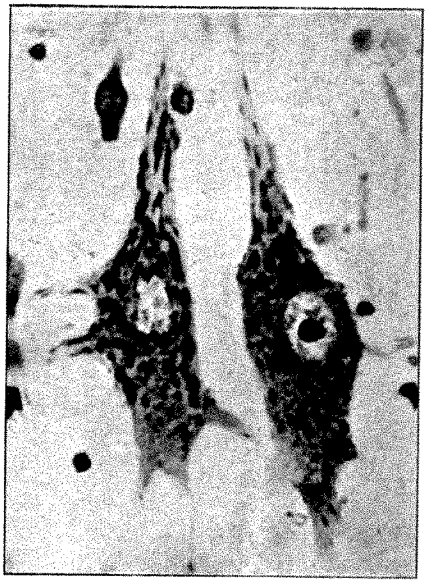

FIG. 2.

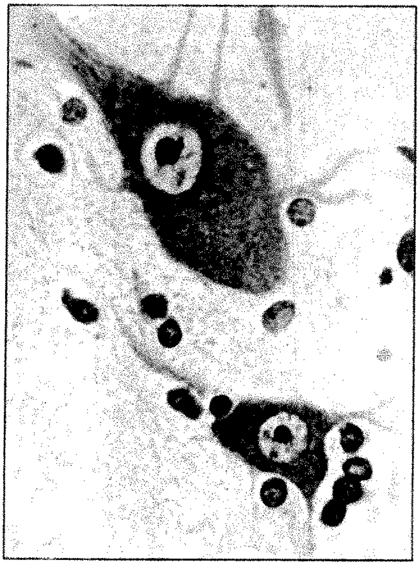

FIG. 3.

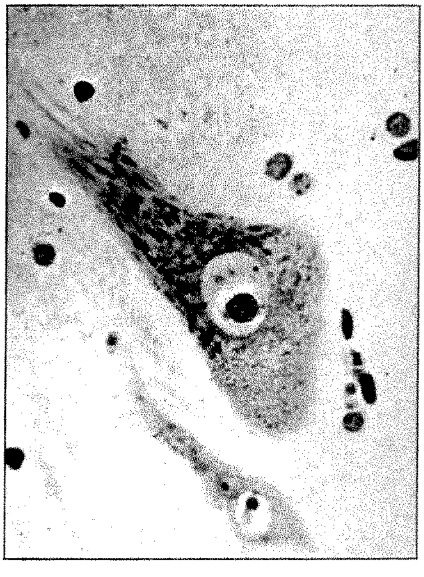

FIG. 4.

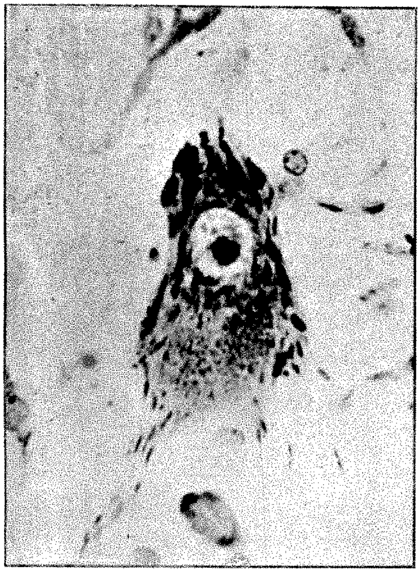

FIG. 5.

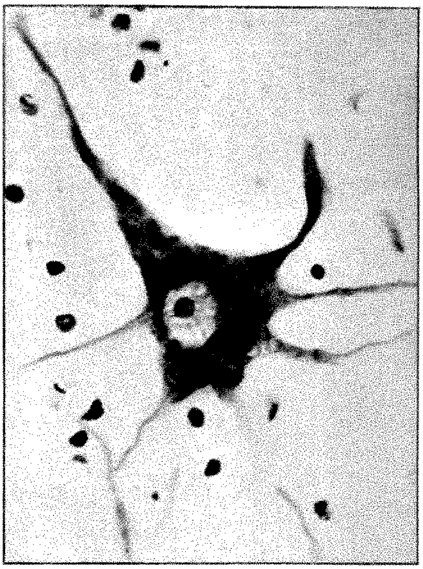

FIG. 6.

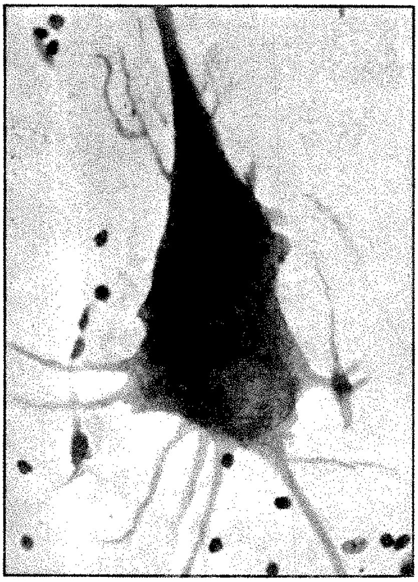

FIG. 7.

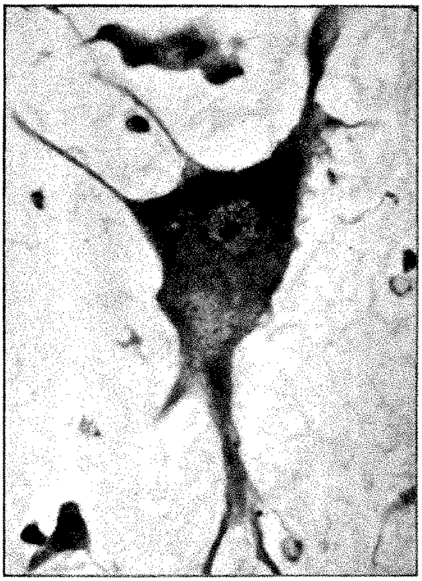

FIG. 8.

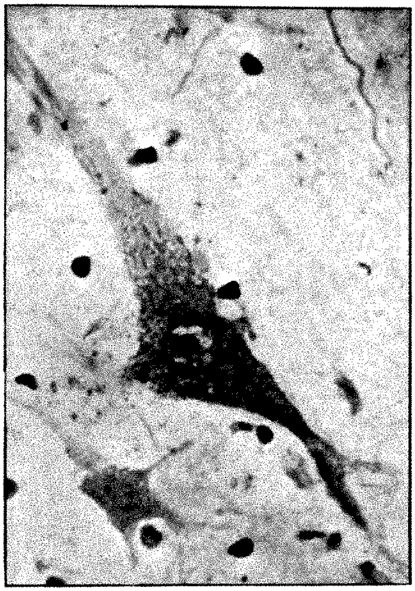

FIG. 9.

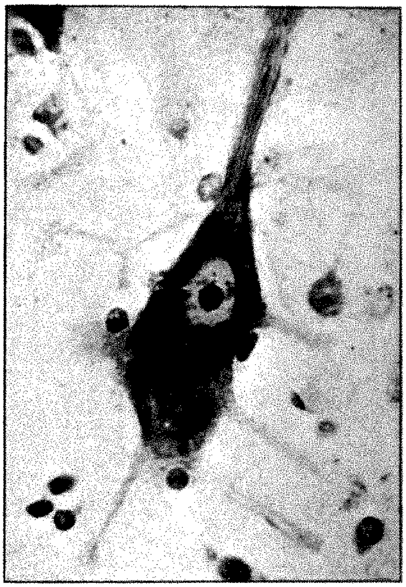

FIG. 10.

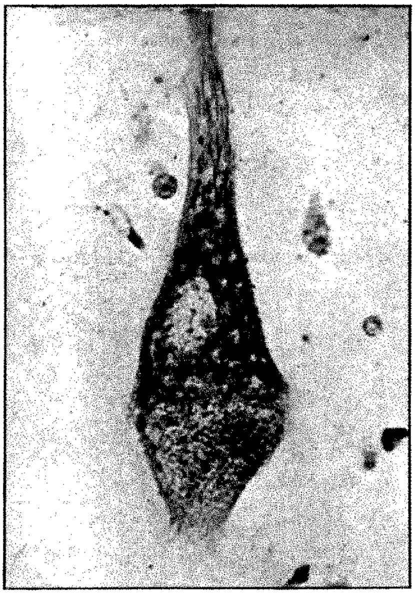

FIG. 11.

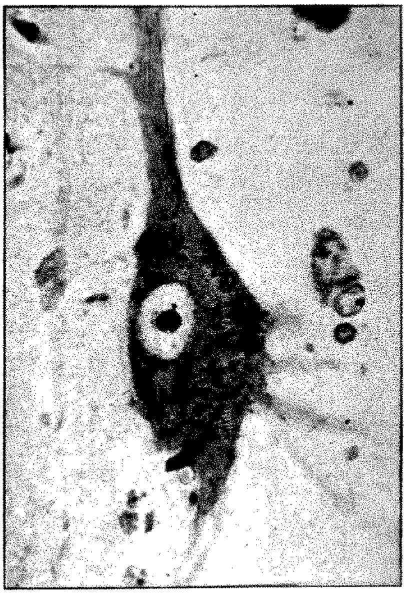

FIG. 12.

ON A FORM OF NERVE TERMINATION IN THE CENTRAL NERVOUS SYSTEM, DEMONSTRATED BY METHYLENE BLUE.*

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SINCE the introduction of the chrome-silver method into nerve histology, our hitherto accepted views upon the relations of nerve-cells have been completely transformed.

The two chief conclusions based upon this method are: first, that axis-cylinder processes and their collaterals, as well as protoplasmic processes, have free terminations; and secondly, that there is no such thing as anatomical continuity of nerve elements.

In 1891 Waldeyer[1] introduced the term *neuron*, which he defined as follows:—"That the central nervous system is made up of numerous nervous units; that the axis-cylinder in every case springs directly from the cell, and further, that all nerve-fibres or fibrils have free terminations by means of tufts or brushes (endbaumchen, endbuscheln). There is no such thing as formation of net or anastomosis."

The first light thrown upon the cellular structure of the central nervous apparatus was in 1865, when Deiters[2] pointed out the distinction between axis-cylinder and protoplasmic processes. His results were soon confirmed by many observers, as Arndt,[3] Schultze,[4] Kölliker,[5] Retzius,[6] and others.

Meynert[7] and Besser[8] believed that the protoplasmic processes of different nerve-cells anastomosed freely with

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* We are much indebted to Professor Ferrier for the opportunities afforded to us for this investigation.

each other. In 1871 Gerlach[9] propounded the theory that a network was formed, composed of afferent fibres and the protoplasmic processes of nerve-cells, out of which arose axis-cylinders. That is to say, there was no real difference between protoplasmic and axis-cylinder processes and the grey matter was a network of continuous strands.

The question may be said to have been left open until the publication by Golgi,[10] in 1875, of his method for impregnating the brain with silver. The conclusions which he deduced were, first, that the network was made up only of axis-cylinder processes and collaterals; and secondly, that the protoplasmic processes were to be regarded as subserving nutrition and had relations with the blood-vessels and ependyma cells.

In 1887 Forel,[11] Retzius[12] (using Ehrlich's original methylene blue method),* and His[13] (by embryological research), were led to doubt the existence of the network, believing in the discontinuity of the elements.

Later, the researches of Ramon y Cajal,[14] Kölliker,[15] van Gehuchten,[16] and Lenhossék[17] confirmed their results, that the grey matter was composed of a feltwork of interlacing but discontinuous fibrils.

In this way arose the present accepted theory of transmission of impulses by contact only.

It would appear, however, as if the varieties of nerve termination, described by those who have largely employed the chrome-silver method, are not the only forms existing in the central nervous apparatus. There is also reason to doubt whether the terminations, described by these observers, are so universal as the study of their writings would lead one to suppose. In 1886 Ehrlich[18] initiated the method of staining nervous tissue by methylene blue. Owing to the exceptional position which Golgi's impregnation method attained, years passed before Ehrlich's method came into anything like general use. Interest in the subject, however, was never entirely lost, and from the first papers on the subject by Aronsohn,[19] until the present day, it has been more and more recognised that in this one has to deal with a method as original as, and perhaps superior to, the impregnation methods of Golgi and Cajal. In fact, the method, if carried out successfully, bears out Ehrlich's original statement: "*That methylene blue possesses an extraordinary relationship to the finest and most delicate branches of axis-cylinder processes, and therefore it is possible to follow out definite nerve endings in the living condition and with a clearness that cannot be attained by any other method.*"

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* Retzius, in invertebrates, injected 0.2 per cent. solution of methylene blue into the body. After a few minutes the central organs were laid bare and exposed to the air. Examination was made from time to time in order to determine the time required for good results. The specimens required to be examined microscopically at once.

In 1895 Bethe[20] discovered that by the use of certain salts—the molybdates—methylene blue could be fixed in the parts already stained. This made it possible to obtain good sections from parts selected for examination. His researches were, however, mostly confined to invertebrate animals. Shortly after this Semi Meyer[21] applied Ehrlich's method to vertebrate animals by means of subcutaneous injections of methylene blue, employing as his fixing agent one of the solutions recommended by Bethe. By this means the brains of even the higher mammals can be thoroughly saturated with methylene blue, afterwards fixed, embedded, and sectioned. If this be carried out carefully and successfully, the structure of the central nervous apparatus is brought out with a clearness that cannot even be attained by the use of the chrome-silver method.

Meyer,[22] in his latest publication, describes a variety of nerve termination which he has met with in various parts of the brain, and comes to the conclusion that it takes the form of a very fine basket of fibrillæ over the cell body and protoplasmic processes. From his preparations, however, no conclusion could be drawn whether this basket-work was made up of a meshwork of continuous fibrils, or of a texture in which each fibril retained its individuality.

He further points out the relations of the dendrites to the cellulipetal fibre. According to Cajal and v. Gehuchten, the protoplasmic processes are the parts of the neuron which receive afferent impulses and conduct them to the cell. Meyer's preparations have led him to believe that there exists no difference between the cell body and protoplasmic processes, the basket-work being as clearly defined on the dendrites as on the cell body, and that the afferent fibre in most instances is found to enter into relation with the neuron near the summit of one of its protoplasmic processes.

This type of termination has been recently noted by Auerbach,[23] Bethe,[24] Golgi,[25] and Held,[26] but from the descriptions given, one is unable to form an idea as to the ultimate behaviour and relation of the cellulipetal fibre to the body and protoplasmic processes of the cell around which it ends.

The use of the chrome-silver method and its modifications is open to objection. In fact, the number of modifications, which it has already undergone, clearly prove the imperfections inherent in it. Being a precipitation method it obscures structure; that is to say, the finer structural details of the elements impregnated cannot be investigated owing to the intensely black deposit on the cells and branches proceeding from them.

The formation of artefacts, the capriciousness of the method, its imperfect durability, and lastly, the defective means it possesses of differentiating nerve-cells from neuroglia cells, constitute additional imperfections. Therefore the use of other methods is necessitated in order to examine in detail the structure of the tissue elements.

It has been noted that most of the imperfections mentioned can be overcome by the use of subcutaneous injections of methylene blue *intra vitam*. This method is much more certain and the structure of nerve-cells, processes, and nuclei can be made out. By the use of methylene blue neuroglia elements are eliminated, nervous tissues only being stained, and medullated as well as non-medullated fibres are defined.

OUR OWN OBSERVATIONS.

The method which has been adopted by us is briefly as follows:—Small quantities of a saturated solution of methylene blue are injected subcutaneously at intervals of from fifteen to twenty minutes until the animal dies. The central nervous organs are rapidly removed, sliced into convenient blocks, and placed in a solution of ammonium molybdate for purposes of fixation. After washing, hardening, and embedding, the blocks are cut as usual and mounted with a cover-glass. Various animals have been employed for this purpose—monkeys, cats, dogs, rabbits, guinea-pigs, and mice. The best results are obtained with rabbits from six weeks to two months old.

Description of the Nerve Termination.—The arrangement which we regard as the termination of a nerve fibre is in the form of a lattice or network surrounding chiefly the cell body. For the sake of clearness this may be described as studied under different powers of the microscope.

(I.) Under $\frac{1}{8}$ inch objective (Swift), and the nucleus of the posterior quadrigeminal body selected for preference.

The terminal is to be found in connection with the large cells of this nucleus, and the following appearances would indicate that we have to deal with a pericellular arrangement (plates i. and ii., figs. 1, 4 and 5).

(*a*) When in clear focus the cell shows a deeply blue-stained peripheral zone.

(*b*) When thrown out of focus the characteristic cell appearance is replaced by a series of fibrillæ radiating over the cell and nuclear region, in connection with which are numerous deeply-stained particles. This is not clearly portrayed until the nucleus is almost invisible.

(*c*) A similar condition may be observed over the roots and main stems of the protoplasmic processes.

(II.) In order to define more clearly the minute structure it is necessary to study the cell under $\frac{1}{12}$ inch oil immersion (Swift), when the following may be seen:—

(*a*) The peripheral zone is found to be nodose and conterminous with the periphery of the cell. At times it presents almost a "thorny" appearance (plate i., fig. 2). When the cell is in clear focus the peripheral zone is found in almost all cases to cross the base of the protoplasmic processes.

(*b*) When the cell is thrown out of focus the fibrillated structure already mentioned is now found to be a lattice work enshrouding the cell (plate i., figs. 1 and 5).

The particles, to which reference has already been made, represent the points of interlacement of the fibrillæ. The general appearance is that of a very fine web or meshwork covering the cell and roots of the protoplasmic processes. In favourably stained specimens, there is one part of the cell in which the lattice work is most clearly seen, namely, over the root of the axis-cylinder process, where, as clearly shown by other methods, there is more or less deficiency in the so-called "Nissl bodies." In these cases the deeply-stained network stands out clearly from the faintly-stained cell background.

The Cellulipetal Fibre.—As far as we have been able to observe, this fibril is characterised by the following appearances (plate i., fig. 3):—

(1) It is a fine, deeply-stained fibre.

(2) On various parts of its course it presents a looped or varicose arrangement, occurring either singly or in pairs, the latter having a characteristic "pair of spectacle" appearance.

(3) From it collaterals are given off at right angles.

(4) It does not present a protoplasmic structure like dendrites.

(5) It never presents a thorny appearance.

(6) In some cases it reaches the cell body by way of the principal stem of a protoplasmic process (plate ii., fig. 3).

(7) There is no evidence of its breaking up into a network before reaching the cell body.

Localities in which the Termination has been found.

(1) *Cerebral Cortex* (plate i., figs. 1 and 2).—According to our experience, nerve-cells take on the methylene blue stain in two ways, whether in the cerebral cortex or in other parts. In all regions which we have examined, deeply as well as faintly-stained cells have been observed.

It is in connection with the faintly-stained cells that we find the terminal arrangement most typically developed; but it is also to be seen in relation with those which take on the stain more deeply.

In successful preparations, numerous examples of the lattice work are to be found in all areas of the cortex, but more especially in that corresponding to the Rolandic area in man. They are limited, so far as we can make out, to the large and small pyramidal cell layers, but there is no clear evidence as to which cells the ending stands in relation. The cellulipetal fibre appears in most cases to run in from the molecular layer and meet the cell near the base of a principal protoplasmic process. We are unable to confirm Meyer's conclusion that the afferent fibre splits up on a protoplasmic process near its summit.

(2) *Optic Thalamus.*—One of the best examples of this type of termination was found in this ganglion (plate ii., fig. 3). The ending was in relation to a large, three-cornered cell of the pulvinar. The cellulipetal fibre joined one of the principal protoplasmic processes at some distance from the body of the cell, but did not break up into a lattice work until it reached the cell body. Before reaching the protoplasmic process this fibre showed distinct thickenings or nodes at irregular intervals.

(3) *Internal Geniculate Body.*

(4) *Anterior and Posterior Quadrigeminal Bodies* (plate i., figs. 4 and 5).

(5) *Red Nucleus.*

(6) *Lateral Fillet Nucleus.*

(7) *Superior Olivary Body.*

(8) *Ventral Auditory Ganglion.*

(9) *Tuberculum Acusticum.*

(10) *Deiters' Nucleus.*

(11) *Dorsal Vago-glossopharyngeal Nucleus.*

(12) *In Motor Cranial Nuclei, namely, Oculo-Motor, Facial, and Hypoglossal.*

In the above-mentioned motor nuclei we have found the endings always in connection with faintly-stained cells, which present characters as regards shape, number, and length of protoplasmic processes, &c., differing from those which take on the stain more deeply, namely, multipolar cells. Meyer has observed a similar condition, and it would appear from our preparations that at least two varieties of nerve-cell are present in those nuclei.

Thus far we have been unable to find this termination in the substantia gelatinosa of Rolando, or in any part of the spinal cord. These are parts of the central nervous system in which, according to the chrome-silver method, so-called nerve endings are specially well seen (Cajal, Kölliker). To account for this discrepancy we are unable at present to offer any explanation.

(13) *Cerebellum.*—Apart from the corpus dentatum cerebelli, no termination of this nature has been discovered. In this latter nucleus the lattice work, surrounding the cell body and principal protoplasmic processes, presents the same characteristics as elsewhere.

Not only does the methylene blue method fail to demonstrate terminations, as we have described, in connection with Purkinje's cells, but there is an entire absence of the structures known as "the pericellular basket-work" and the "fibres grimpantes," described by Ramon y Cajal. As the staining property of methylene blue is purely confined to nervous elements, neuroglia and connective tissue being unaffected, we would argue that these arrangements are of a non-nervous nature.

As is well known, by the use of the chrome-silver method, the formation of artefacts, namely, the spread of deposit, the staining of the lymph case, and the degree of impregnation depending upon the texture of the tissue, is of frequent occurrence in the cerebellum. We are, therefore, inclined to believe with Hill[27] that the pericellular baskets and "Kletterfasern" surrounding Purkinje's cells and processes are not the end terminations of nerve fibrils.

Further, the "fibras musgosas" (mossy fibres) are shown to great advantage by means of this *intra-vitam* method, the thickenings or rosettes being very clear in outline in well-stained preparations.

In no case, however, have we been able to demonstrate endings around the granule cells, as described by Dogiel, nor can we support the hypothesis of Cajal, that the dendrites of the granule cells break up over the bodies of their neighbours.

(14) *Nucleus of the Corpus Trapezoides* (plate i., fig. 3).—This nucleus, described by Held[28] and Kölliker[29], occupies a position in the ventral part of the tegmentum, between the superior olivary body and the roots of the abducens.

Kölliker, with the chrome-silver method, described the cells of this nucleus as being round or spindle-shaped, and possessing axis-cylinders which proceeded from the cell body by means of a number of small, thick branches, fusing at some distance to form the efferent fibre. At first he declared this to be an artefact, but in his later publications regards only the thickness of the fibres to be due to artificial production. That this appearance was not the commencement of axis-cylinder processes, but really the end termination of nerve-fibrils, was first pointed out by Held. Later, the researches of Cajal[30] and Meyer[31] have placed the matter beyond dispute.

According to Meyer, these afferent fibres, just before ending, become gradually thickened, and near the cell break up into a variable number of branches, which clasp the cell, forming a basket or shut cup. Cajal, however, has come to the conclusion that no basket is formed, but the ending is to be regarded as an open cup, or, as he terms them, "löffel formige plaques."

Our own observations tend to confirm Meyer's conclusions, namely, that it is the most easily demonstrable end termination in the central nervous system; that it takes the form of a network enveloping the cell body, and, finally, in opposition to Held, that there is no direct continuity between the termination and the protoplasm of the enshrouded cell.

Conclusion.

For the following reasons we would urge our belief that the above described arrangement is really the termination of a nerve fibre:

(1) That in the majority of cases a cellulipetal fibre may be traced to, and found to break up over, the cell body and base of the protoplasmic processes. In no case has the cellulipetal fibre been found to break up previous to reaching the cell body.

(2) That this lattice-work is most clearly defined over that portion of the cell, namely, the root of the axis-cylinder process, which is deficient in the so-called Nissl bodies.

(3) That it is also clearly seen over cells whose general staining is faint.

(4) That when the cell is rendered indistinct by changes in the focus, the lattice-work is thrown into clearer perspective.

(5) That, as best seen in the nucleus of the trapezium, the ending may be apparent without the cell.

REMARKS.

The variety of nerve-termination just described is in complete harmony with the neuronic theory of nerve elements, at present holding the field in nerve anatomy; that is to say, the neuron is a unit, discontinuous with adjacent neurons, and conveying impressions by contact and not continuity of tissue. This termination, demonstrated by means of *intra-vitam* injections of methylene blue, is in the form of a fine lattice-work, forming the extremity of the axis-cylinder process of one neuron, enshrouding the body of the neuron next in order. Although physiologically more or less in harmony, this is really anatomically at variance with the descriptions given by Golgi, Cajal, and others, of the ultimate termination of nerve-fibrils. These observers have worked chiefly with the chrome-silver method, which, being a *post-mortem* impregnation process, obscures structure and does not allow the finer details to be investigated.

With the exception of the pericellular basket-work and "Kletterfasern" around Purkinje's cells in the cerebellum, to which further reference will presently be made, the generally accepted doctrine is as follows: first, that the "terminal" consists of a tuft of nerve-fibrils whose extremities may be in some pointed, in others knob-like; secondly, that in the meshwork in the grey matter, which is thus formed, these come into contact with the arborisations of the protoplasmic processes of cells; and thirdly, that nerve impulses are transmitted from the terminal tuft along these protoplasmic processes to the cell body, and thence to the axis-cylinder. Our conception of the method of transmission of impulses from one neuron to another, in view of what we have observed, is a modification of that currently held. From the fact that the cellulipetal fibre breaks up into a network in relation with the cell body, and that the mesh cannot be traced for more than a short distance over the chief trunks of the protoplasmic processes, we assume that the impulses are transmitted from the terminal directly to the cell body and thence to the axis-cylinder.

What the function of the protoplasmic processes may be is less clear. Golgi traced the protoplasmic processes into connection with the blood-vessels and ependyma cells, and regarded them as subserving nutrition. Cajal and v. Gehuchten believe that they alone are the chief collectors of impulses and conduct them to the cell body.

According to S. Meyer, who has worked with the methylene blue method, the terminal arrangement is found over the whole extent of the protoplasmic processes and cell body. He therefore concludes that there exists no real difference between the cell body and protoplasmic processes, a view which receives support from a study of ganglion cells, after staining by the Nissl method, by which it is seen that the chromatic granules are found in the protoplasmic processes and cell body, but not in the axis-cylinder.

From our own observations, however, we would incline to the old view of Golgi, that their chief function is nutritional, or, at all events, of a different functional nature to the axis-cylinder process. In support of this theory, Bethe and others have recently demonstrated by other methods that certainly the protoplasmic processes and perhaps the nucleus and protoplasmic accumulations of the ganglion cell subserve nutrition.

As already incidentally mentioned, the only structures comparable to what we have described, detected by the Golgi-Cajal method, are the so-called "basket arrangements" round the Purkinje cells in the cerebellar cortex. Cells are described, situated in the molecular layer, whose axis-cylinder processes and collaterals end in a brush of fibrils, which form a basket investing the body of a Purkinjé cell. As the end filaments approach these cells, each of them divides into a brush or basket, in which, however, each fibre, according to Cajal and v. Gehuchten, retains its individuality. From the fact that there is no evidence of these structures on *intra-vitam* staining with methylene blue, and also that they do not form a lattice-work of continuous fibrils in any way comparable to that which we have described in other parts, we do not regard them as of a nervous nature, but neuroglial. Hill's conclusions as to the drawbacks to the chrome silver method, namely, spread of deposit, staining of the lymph case, and the open nature of the tissue around Purkinje cells, together with the fact that by the use of methylene blue neuroglia elements are eliminated, strengthen our belief as to the neuroglial nature of the basket arrangements and "Kletterfasern" around Purkinje's cells.

In conclusion, control observations by means of *post-mortem* methods have failed to demonstrate this lattice or network termination. It would seem necessary that, in order to obtain any idea as to the ultimate subdivisions of nerve-fibrils, the tissues should be given the opportunity of selecting the stain during life.

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PLATE I.

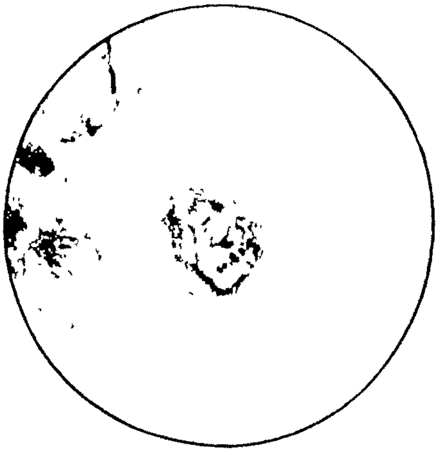


FIG. 1

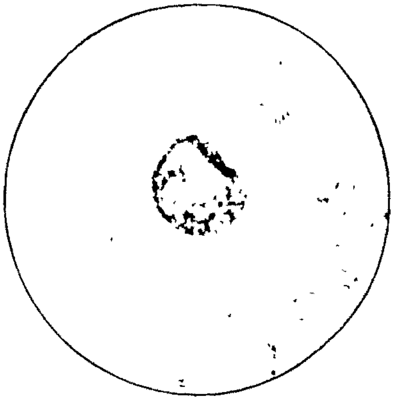


FIG. 2.

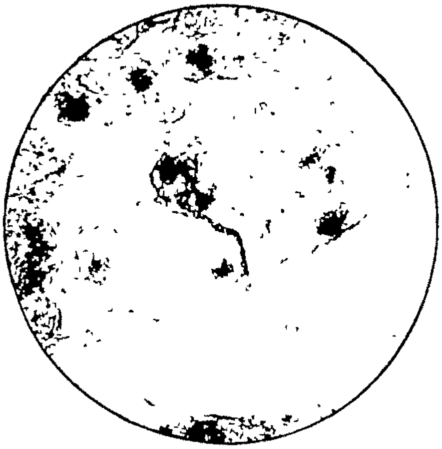
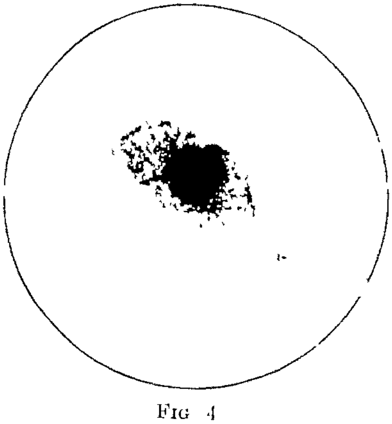


FIG. 3



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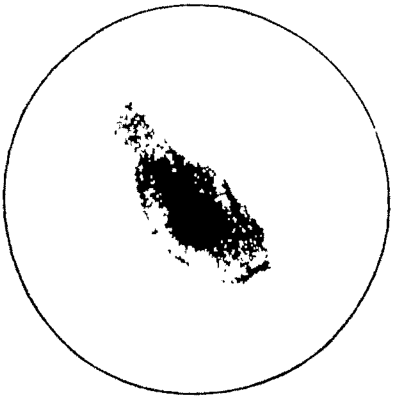

FIG. 5

PLATE II.

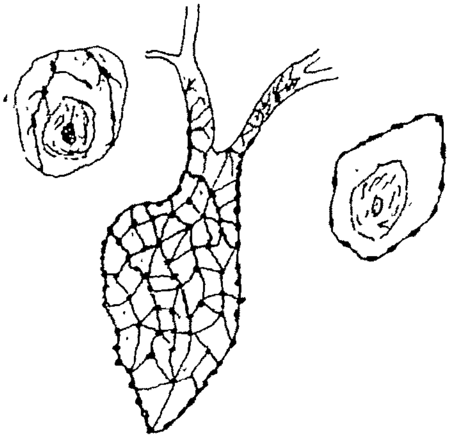

Fig 1.

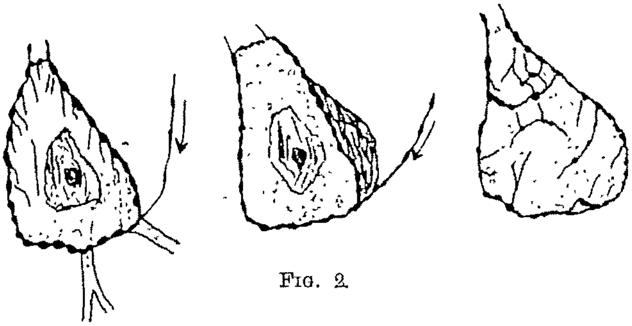

Fig. 2.

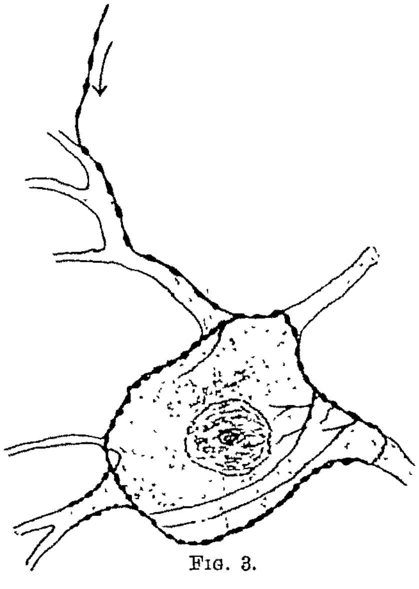

Fig. 3.

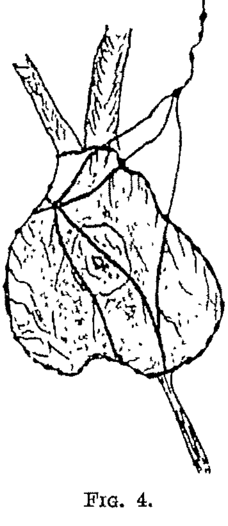

Fig. 4.

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EXPLANATION OF THE PLATES.

We are indebted to Mr. J. E. Barnard for the photo-micrographs, which have been taken from our original preparations.

PLATE I.

Photomicrographs, illustrating the form of nerve termination described in the text.

FIGS. 1 AND 2.—Swift ⅛ dry objective. No. 2 ocular. Camera extension, 7 feet. 750 diameters. A nerve-ending from the cerebral cortex of a guinea pig; fig. 1 shows the network in focus; fig. 2, the peripheral zone in focus. In this termination there is no obvious evidence of a cell.

FIG. 3.—Swift ⅛ dry objective. No. 2 ocular. Camera extension, 7 feet. 850 diameters. A nerve-ending from the nucleus trapezoides of a rabbit. Here the cellulipetal fibre is seen breaking up into a basket arrangement and enclosing a cell.

FIGS. 4 AND 5.—Same magnification as figs. 1 and 2. A cell from the nucleus of the posterior quadrigeminal body of a rabbit, enclosed in the terminal net-work. These figures show the appearances presented on altering the focus, so as to reveal *(a)* the peripheral zone, *(b)* the enshrouding network.

PLATE II.

Diagrammatic representations of the termination and cells.

FIG. 1.—Cell from posterior quadrigeminal body.
FIG. 2.—Cells from cerebral cortex.
FIG. 3.—Cell from optic thalamus.
FIG. 4.—Cell from cerebral cortex.

A CONTRIBUTION TO THE LOCALISATION OF MUSCLES IN THE SPINAL CORD.

BY H. CAMPBELL THOMSON, M.D.LOND., M.R.C.P.

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DURING the past three years I have had numerous opportunities of examining cases of injuries to the spinal cord, some of which have been particularly instructive with regard to the relative localisation in the grey matter of muscles of the upper extremity.

The cases which I have found most valuable for this purpose are those in which the chief injury has apparently been due to hæmorrhage into the grey matter, for in many of these the lesion is sharply localised, and by careful comparison of the muscles which are affected in different cases, some conclusions may be arrived at regarding the different levels from which the muscles are supplied, and a finer analysis is thus more possible than in cases where the injuries are more diffuse.

An interesting case of this description was admitted into the Middlesex Hospital in 1897, under the care of Mr. Henry Morris, who kindly allowed me to make use of the notes.

The patient was a man who had injured his spine by diving into a swimming bath and striking his head against the bottom.

On admission there was weakness of all four limbs, which was rather more marked on the right side than on

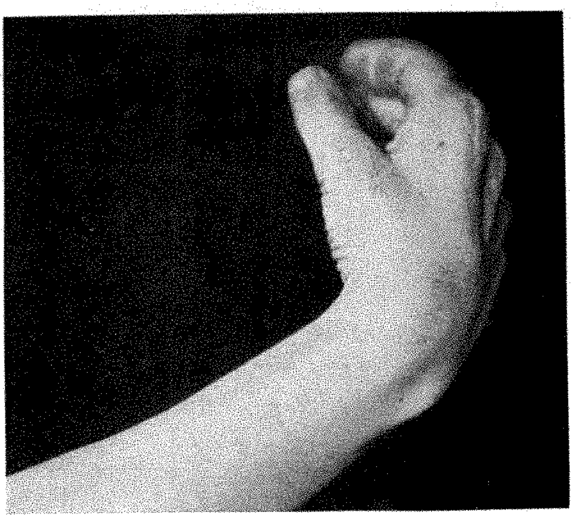

Fig. 1.
Showing power of flexing the wrist.

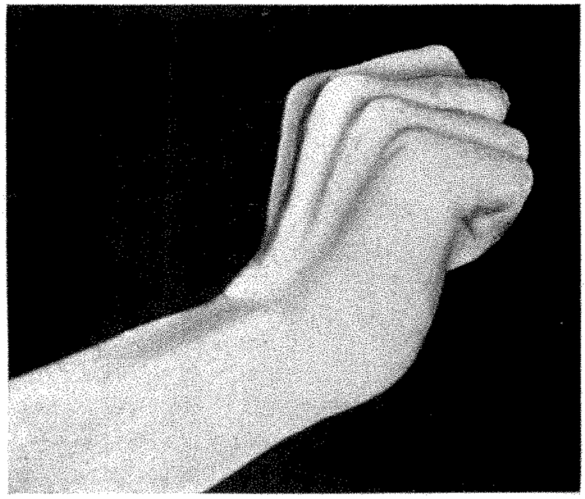

Fig. 2.
Showing over extension of wrist when attempting to flex the fingers.

the left, and it was also noted that the right hand seemed quite helpless.

Within a day or two the general weakness of the limbs almost entirely passed off, but the paralysis of the hand remained.

On examination the movements of the wrist joint were found to be normal (figs. 1 and 2), but there was complete loss of power in all the muscles attached below this level, *i.e.*, the long flexors and extensors of the fingers and thumb; the interossei and the small muscles of the thumb. No movement whatever could be made with these muscles, and whenever flexion of the fingers was attempted, a very strong over-action of the extensors of the wrist took place (fig. 2).

Rapid wasting also occurred in the paralysed muscles.

In a short time, however, some improvement began to take place, especially with regard to the long flexors of the fingers and the small muscles of the thumb, and both these groups acted to a moderate faradic current, but the power of flexing the first finger remained less than that of the other three.

The long extensors of the fingers and thumb and the interossei did not, unfortunately, join in this recovery, but gradually wasted and lost their irritability to the faradic current.

After the patient was able to leave the hospital he attended regularly for some weeks to receive electrical treatment, but finally, at his own request, this was discontinued.

At the time he ceased attending, it was evident that no further recovery was very likely to take place, and the condition was as follows:—

The long extensors of fingers and thumb The interossei	... Remained paralysed.
The long flexors of fingers and thumb	Partially recovered.
The small muscles of the thumb	Recovered.

With regard to the nature of the lesion in this case, there was no doubt a slight transverse injury to the cord at the time of the accident, as shown by the temporary paralysis of all four limbs, but the more permanent effects were in all probability caused by a localised hæmorrhage into the grey matter which evidently chiefly affected those nuclei which govern the muscles of the hand, and caused no disturbance of sensation beyond some slight thermal anæsthesia, such as so often accompanies a lesion of this description. The interest of the case, with regard to the localisation of muscles, lies in the fact that while the muscles of the wrist entirely escaped, all those below it were more or less affected, and we therefore see that the nuclei which supply the long flexors and extensors of the hand are definitely separated from, and probably situated at a lower level than, those which supply the muscles of the wrist-joint.

A comparison of this case with another one of a somewhat similar nature, which, through the kindness of Mr. Andrew Clark, I have recently had an opportunity of examining, further shows the relative position which the nuclei of the long extensors and flexors occupy in the spinal cord.

The case was one in which there was wasting of the muscles of both hands, accompanied by extensive loss of thermal and painful sensations, while those of touch were preserved, and therefore, like the first case, the lesion was probably one of hæmorrhage into the grey matter. But, whereas in the first case the long flexors and extensors of the fingers were affected with the small muscles of the hand, while the muscles of the wrist escaped; in the second case the small muscles of the hand were alone affected, and the long extensors and flexors escaped completely.

The fact that in the one case the flexors and extensors of the fingers shared the same fate as the small hand muscles, and in another shared the fate of the wrist muscles, clearly points to the supposition that their nuclei are placed in an intermediate position between those of the other two.

The result of the first case also suggests that there is probably a close relation between the long extensors and the interossei, since these were the two groups which remained permanently paralysed.

Another case of injury to the spinal cord, the notes of which I have unfortunately mislaid, led me to think that the motor cells for the extensor carpi radialis are situated at a higher level than those of the extensor carpi ulnaris.

The following diagram illustrates the relative positions of the various nuclei as suggested by the cases which I have observed.

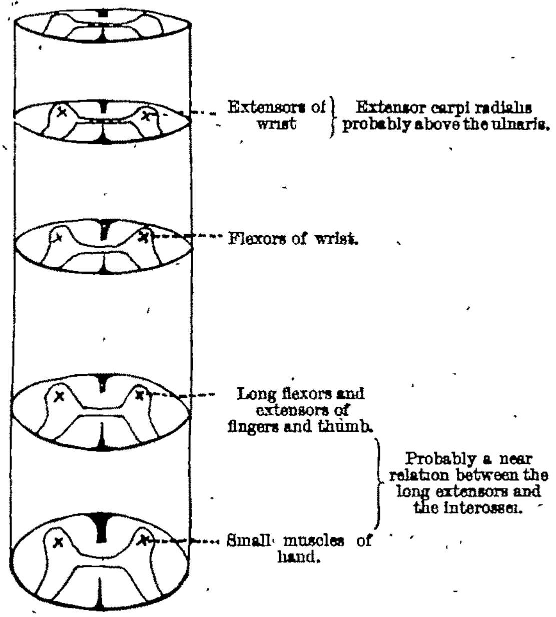
Extensors of wrist
Extensor carpi radialis probably above the ulnaris.
Flexors of wrist.
Long flexors and extensors of fingers and thumb.
Probably a near relation between the long extensors and the interossei.
Small muscles of hand.

Fig. 3.

It is generally assumed that the group of muscles supplied by a given root is the same as that supplied by the corresponding segment of the spinal cord; but this is not necessarily so, and the above cases indicate that the representation of muscles in the cord is much more widely distributed than that of the roots, and that the latter are made up of fibres converging from their anterior cornua at different levels of the cord.

With regard to the root distribution, according to most clinical records the extensors of the wrist and fingers are supplied from the seventh cervical root, the flexors of the wrist and fingers from the eighth, and the interossei and other small muscles of the hand from the first dorsal, whereas the cases above quoted show that in lesions of the anterior cornua the flexors and extensors of the fingers may be affected independently of the muscles of the wrist, and also independently of the small muscles of the hand.

HYPNOTISM: A REPLY TO RECENT CRITICISMS.

BY J. MILNE BRAMWELL, M.B.

At the present day, although the reality of hypnotic phenomena is generally conceded, wide differences of opinion exist as to the nature of hypnotism, and its value and safety as a therapeutic agent. Thus, in "Hypnotism in Court" and "Hypnotism," two articles which appeared in the July and October numbers of the *Journal of Mental Science* for 1898, the views expressed are not held by the majority of those who practise hypnotism. As the articles referred to, both apparently from the same pen, are unsigned, I will, for convenience' sake, call the writer X.

First, I wish to draw attention to a personal point; X, in referring to my address to the Psychological Section of the British Medical Association, says: "The bold attempt of Dr. Milne Bramwell to prove there are no drawbacks to the therapeutic use of hypnotism is, however, a challenge which should be promptly met." Now I have never, either in writing or speaking, asserted that there were no drawbacks to the therapeutic use of hypnotism, but, on the contrary, have constantly pointed out that many existed. For example, in this country hypnotism is rarely resorted to until other remedial measures have failed, and this greatly decreases its chance of success. Further, I have never denied that hypnotism, through ignorance or malice on the part of the operator, might be so misused as to do harm; this risk, however, is not only grossly exaggerated, but falls far short of that associated with ordinary medical practice.

What I really said was totally different, namely, that, as far as my experience went, the employment of hypnotism by medical men acquainted with the subject was devoid of danger. In support of this I cited Forel's assertion that he, as well as Liébeault, Bernheim, Wetterstrand, van Eden, de Jong, Moll, and the other followers of the Nancy school, had never seen a single instance in which mental or physical harm had been caused by hypnosis. No complete record of their cases has been published, but the number certainly exceeds fifty thousand. On October 15, 1898, Forel informed me that he still held this opinion, and had never observed even the slightest inconvenience from hypnotic practice. Further, I have watched the work of nearly all of those cited by Forel and have seen nothing opposed to his statement.

I could add many names to Forel's list, but will content myself by quoting one or two in this country, choosing them for their connection with asylum practice.

In 1890, Dr. Percy Smith and the late Dr. A. T. Myers published an account of the hypnotic treatment of twenty-one insane patients in Bethlem Hospital, I am authorised by the former to state that no harm was done.

Dr. Woods, of Hoxton House Asylum, has hypnotised over a thousand persons, many of whom were insane. He recently informed me "that he had never in his own practice seen any evil effects, either mental or physical, caused by the use of hypnotism."

I have also Dr. Outterson Wood's permission to state that, while he acted as Honorary Secretary to the British Medical Association Committee for the Investigation of Hypnotism, he performed several hundred experiments and arrived at the following conclusions with regard to hypnotism:—(1) Its phenomena were genuine; (2) It was of distinct therapeutic value; (3) Its use in skilled hands was absolutely devoid of danger.

My position might be attacked in two ways: (1) By attempting to prove mal-observation; (2) The facts being granted, by showing that they did not warrant the conclusions drawn from them. These, the only two points at issue, X entirely ignores. He says: "Very many observers have seen cases in which hypnotism has been followed by very definite and distinctly evil results. Many instances of this kind have been recorded, and good service would be done by their collection and tabulation, as a check to future assertions of this kind." Granting that this be true, what connection has it with the point in dispute? If a group of surgeons performed a certain operation fifty thousand times without a death, would they not be justified in inferring that in their hands, at all events, it was devoid of danger? Would their position be weakened by the "collection and tabulation" of the failures of others?

There remain for discussion the hypnotic dangers referred to by X, namely (1) evil results recorded by other observers, and (2) those occurring in his own practice.

(1) Harm reported by others.

As regards this group, X does not cite a single authority or case; surely the "collection and tabulation" to which he refers should have been done beforehand, and the results presented in such a way as to enable one to judge of their value as evidence.

I have investigated every case brought to my notice where hypnotism was stated to have done harm, and in none has the charge been proven. The two following may serve as a commencement of the collection X is desirous of making:—

(*A*) A patient, suffering from torticollis, who had been under my care for a few weeks, shortly afterwards underwent a surgical operation; an important blood-vessel was accidentally cut and about ten days later she died from secondary hæmorrhage. I was informed that the surgeon asserted the hæmorrhage and death were due to the fact that the patient's constitution had been weakened by hypnotism. If this were true, the relatives felt that they had contributed to the death by permitting the patient to try hypnotic treatment, and I was asked whether I could in any way reassure them. This I had little difficulty in doing. I informed them (*a*) that hypnotism did not weaken the constitution; under its influence Esdaile had reduced the mortality in the removal of the tumours of elephantiasis from 50 to 5 per cent., and my own operative cases had all done well; (*b*) even granting that hypnotism could weaken the constitution, it was unreasonable to suppose that it had spread from the patient to the surgeon and thereby caused him to accidentally cut a blood-vessel; (*c*) I mentioned the not unimportant fact that I had absolutely failed to hypnotise the patient.

(*B*) In April, 1897, a medical acquaintance told me I must alter my views as to the dangers of hypnotism, because, by its means, M., a Swiss medical man, had seduced eleven young female patients and had been condemned to five years' imprisonment. One of the victims, I was told, had committed suicide, and before doing so, had left a written statement of the fact that she had been seduced through hypnotism. Further, I was informed that these statements were confirmed by ample official evidence. This I asked to see, and received what was described as "the official testimony from Dr. Calonder, of the 'Advokaturbureau,' in Chur, where the case was tried, stating that hypnotism had been abused in this shocking betrayal." My colleague continued, "I could also send you the four German newspapers sent me; but as they contain no details which I have not given you, you probably would not care to have them."

The following is a translation of the document in question:—"In reply to your favour of the 26th inst., I hasten to inform you that, at the trial of Dr. M., no support was found for the assertion that he had employed hypnotism in the treatment of his patients.—(*Signed*) Dr. Calonder."

I asked for the German newspapers, and found that in the account of the trial hypnotism was not even mentioned. I then laid the matter before Professor Forel, of Zurich, who replied as follows: "Dr. M. has never hypnotised a patient. The question was not raised at the trial, and no one suggested that he had employed hypnotism. The entire history is an English invention. In Zurich no one has spoken or written of hypnotism in connection with Dr. M. He is a throat specialist—an ordinary erotic pig, and has long been known as such. I have written to the Judge of the Supreme Court, who tried Dr. M., and he has sent me a written statement which confirms mine; this I now enclose, so that you may have a trustworthy document." Prof. Forel's letter and that of the Judge are still in my possession. They describe Dr. M.'s methods of seduction, but as these have nothing to do with hypnotism, and are not particularly fit for publication, I refrain from quoting them.

(2) X's Cases.

X says, in his special department, presumably asylum practice, the evils consequent on hypnotic influence are grave, and that the few cases in which it seemed desirable to induce hypnosis, were, in the end, apparently deteriorated in mental condition, and that the conservation of mental power, so urgently indicated was, in fact, endangered. From this he concludes that hypnosis involves a weakening of the power of self-control, and "is indeed, a shunting on one of those side tracks of disordered mental function of which insanity is the terminus." Here I may point out (1) that no figures are given, and the word "few" is an indefinite one; (2) the disease from which the patients suffered is not stated, nor the absolutely essential information given whether it was one likely to end in mental deterioration apart from the treatment; (3) X does not assert that mental deterioration resulted from hypnosis, but only that it apparently did so; (4) although X practically states that hypnosis leads to insanity, he does not tell us that insanity was actually produced.

It is to be regretted that X gives no detailed account of his cases, as thus, the dangers to which he refers are based more upon assertion than upon evidence which might be examined and judged. Granting, however, that mental deterioration actually resulted from X's hypnotic practice, one cannot help feeling that his personal and limited experiments do not warrant the conclusions he draws from them. Fortunately, it is not a recognised principle in medicine that those who fail have the right to cry "Halt!" to the successful.

According to X, hypnotism is related to hysteria, stupor, latah, &c.

(I.) *Hysteria.*—The supposed connection between hypnotism and hysteria, disputed by Esdaile and Braid more than fifty years ago, was restated by the Salpêtrière school, and successfully disproved by that of Nancy. X's attempt to revive an ancient fallacy is not likely to be successful; especially as he does not support it by a single observed fact.

At the International Congress of Experimental Psychology, London, 1892, it was generally recognised that susceptibility to hypnosis did not indicate hysteria or any other morbid condition in the subject. Hypnotism was found to increase the patient's volition; thus the cure was due to the intensification of an entirely normal moral process, and was not really dependent upon assistance from without. It is true, as Myers has pointed out, that a superficial resemblance exists between the phenomena of hysteria and those of hypnotism. In hysteria certain nervous, vasomotor and circulatory changes arise, apparently as the result of irrational and unconscious self-suggestion in regions beyond the power of the waking will. The hypnotic self also can influence the nervous, vasomotor and circulatory systems to an extent unparalleled in waking life. Here, however, the phenomena are under the subject's own control, and he can be taught to evoke and terminate them at will.

According to X, self-control is weakened in hypnosis. This view is an old mesmeric fallacy which was successfully exploded by Braid fifty years ago. My patients, no matter how deeply hypnotised, can always choose between suggestions and reject what is distasteful. The supposed loss of self-control is assumed by the operator from the observation of laboratory crimes. Questioning in hypnosis, however, reveals the fact that there has been neither loss of consciousness nor of volition. This view I have put before the profession from time to time, and most of the experiments on which it is founded have been carefully checked by others. Some of these, carried out in conjunction with Dr. Hyslop, of Bethlem, are recorded in his work entitled "Mental Physiology."

X asserts that therapeusis admits the principle that lower tissue may be sacrificed to save a higher, but that it is distinctly bad practice to harm the higher organ to release the lower, as hypnotism does. This concerns ordinary rather than hypnotic practice. Most of the diseases which are treated hypnotically are central in their origin, as, for example, dipsomania, hysteria, obsessions, &c. In such cases it is the relief or cure of the higher organ which is at stake, and no sacrifice of any kind, either higher or lower, is involved. Lost or weakened self-control is at the root of the diseases just referred to, and, when hypnotism cures them, it does so by developing the patient's own volition.

If, however, we judge ordinary practice by X's standards, the administration of narcotics and anæsthetics must be condemned, and their employment for the relief of pain considered bad practice. X's opinion, I think, is not now generally held by the profession, although, in 1842, Dr. Copland asserted, at the Royal Medical and Chirurgical Society, that "pain was a wise provision of nature, and patients ought to suffer pain while their surgeons were operating; they were all the better for it, and recovered better."

(II.) *Stupor.*—Stupor has been divided into two forms—(1) Anergic and (2) Delusional.

(1) Anergic.—In typical cases there is blueness and swelling of the hands and feet, slow and feeble circulation, vacant expression, retention (in some cases incontinence) of urine and fæces, complete absence of mental function in the region of will, perception, memory, and often even of consciousness.

(2) Delusional.—This form is the outcome of profound melancholia, in which the mental activity is terminated by a melancholic delusion.

Stupor is supposed to be due to pathological changes in the brain and its blood-vessels; it is generally associated with grave disease and frequently has a fatal termination ("Dictionary of Psychological Medicine," Hack Tuke).

Again X contents himself with simple assertion, and omits to adduce a single fact in support of the supposed connection between stupor and hypnosis. Hypnotised persons do not turn blue, nor do their hands and feet swell; they do not lose control over the bladder or bowels. Their volition is unimpaired, their perception and memory are often abnormally acute and consciousness is rarely, if ever, lost. Hypnosis is not associated with profound melancholia, nor does it end in a cessation of mental activity. On the contrary, the hypnotised person may be able to solve mental problems of great difficulty which are beyond the range of his normal powers. Again stupor, unlike hypnosis, cannot be originated, guided or terminated at will. Further, hypnosis does not arise from pathological changes in the brain and its blood vessels, nor has it a fatal termination.

(III.) *Latah.*—X talks of latah as if it were a disease, but, as Moll has pointed out, the word latah designates the sufferers from the complaint, not the disease itself. Latah, according to Gilles de la Tourette, is a "tic" characterised by certain abnormalities of movement, particularly the imitation of gestures, and by certain anomalies of speech, such as the use of bad language, and the repetition of the last words uttered in the patient's presence. Bamberger states that violent contractions of the flexors and extensors of the muscles of the leg take place when the patient attempts to stand, and thus a jumping movement is produced.

According to Clifford and Talcott Williams, the condition is latent in the Malay race and can be induced by startling them and making them jump. They will then imitate actions which are painful, dangerous, or obscene. The Malays are a race particular to a fault about all matters of personal modesty, but a latah Malay woman will strip naked in a public place at the casual invitation of a passing stranger.

In attempting to establish an analogy between hypnotism and latah, X, as usual, states an old fallacy without adducing a single fact in support of it. His theory is apparently a reproduction of that of Dr. Gillmore Ellis (*The Journal of Mental Science*, January, 1897, p. 32). Neither writer seems to be aware of the fact that similar views were expressed at an earlier date by several Continental observers, and their unsoundness demonstrated by Moll and others. The fallacy appears to have arisen from untrained and superficial observation. Thus, it has been noticed that both the latah Malay and the hypnotised person imitate gestures; the conditions, therefore, are assumed to be similar.

The circumstances, however, under which they do so are widely different. The moment a "latah" is startled he will at once imitate any gesture made before him by anyone. He will also mimic the swaying motion of wind-shaken boughs as readily as the actions of a human being (Clifford). No verbal suggestion is necessary. On the other hand, hypnotised subjects never copy movements made before them unless they have been trained to do so, and then only those of the hypnotiser. Again, hypnotised persons, even despite energetic suggestion, will not imitate actions which involve real danger, actual indelicacy, or obscenity, nor do they make use of bad language. Further, the hypnotic subject, unlike the latah, does not hop about like a kangaroo the moment you startle him. Moreover, hypnosis can be terminated at will, but the disease from which the latah suffers is uncontrollable and frequently incurable.

Other writers besides X have attempted to establish a connection between hypnosis and many and widely differing diseased conditions. In every instance the fallacy has been due to the imperfect observation of some isolated hypnotic phenomenon. Benedikt's theory is fairly characteristic of this class. In his view of hypnosis, its numerous, varied and complex mental and physical conditions are ignored, and it is simply classified as an artificially induced catalepsy, because in hypnosis the muscles can be rendered rigid by suggestion.

Such theories have the merit of simplicity, and possess the additional advantage that they can be made without careful observation or prolonged study. What should we think, however, of the observer who described normal human life as simply an artificially induced sneeze, because the act of sneezing could be readily invoked by the presentation of a pinch of snuff!

Moll draws attention to the fact that hypnosis has been compared to the most dissimilar forms of mental disease. Those who do so, he says, forget amongst other important things that susceptibility to suggestion is the chief phenomenon of hypnosis, and that this is far from being an essential characteristic of mental disorder. We can produce paralysis, stammering, or pain by suggestion, but hypnosis itself is none of these things. Moll points out that it is illogical to call hypnosis a disease because morbid imitations of it are found. Yawning itself is not a disease, although attacks of it occur, which are morbid in character. Thus, we are no more justified in inferring that the hypnotised subject suffers from hysteria because he can imitate its symptoms than in concluding that an actor is mad when he portrays insanity. Further, hypnosis is entirely under the control of the operator, or of the subject himself, but there is no disease which can be originated, guided and terminated at a moment's notice.

Faith-healing.—X asserts that "therapeutically hypnotism is related to various forms of faith-healing, the limitations of which are fairly well-known and recognised." X does not define faith-healing, and it may be useful to supply his omission.

According to the Bible, the power of healing is one of the attributes of the Deity which is at the service of those who solicit it, and believe their prayer will be granted. Here two factors are involved, the power to cure possessed by the operator and faith on the part of the patient. The former may be eliminated from present day faith-healing, which is essentially characterised by a belief in what does not exist, *i.e.*, the curative power of the operator. X's theory, that hypnotic phenomena are due to emotional states associated with faith, was held by Braid in the earlier part of his career, and is still regarded as correct by certain later observers. Recent investigations, however, have done much to discredit this view, and a short account of its origin, together with the changes which have since taken place in hypnotic theory may not be without interest.

In Braid's day, so-called mesmeric phenomena were supposed to be due to external agencies, *i.e.*, a mysterious force existing in the operator, and in various metals, magnets, &c. Braid showed how identical phenomena could be induced in the absence of the supposed exciting causes, if the patients were led to believe that these were present. For example, the cures attributed by Dr. Perkins to the action of his "metallic tractors" were equally successfully obtained by Dr. Haygarth's pieces of wood. Braid concluded that in all these things faith, expectation and concentrated attention were the only curative agents. Further, he thought, the action of medicines might partly be explained in the same way, and that the mental element associated with their administration had been far too much ignored. All medicines had a two-fold action; one due to their physical properties, the other to the patient's expectation of a definite result. This mental impression accounted for the varying estimates as to the value of certain drugs. Thus, at one time a universal favourite was supposed to cure everything, then was regarded as valueless, only later to regain its former position. The drug itself did not change, only the belief or confidence of those who prescribed, and those who took, it.

Elliotson also pointed out that, owing to the mistaken way in which medicines were frequently administered, their curative effects, if any, must be due to the faith of the patient. Some physicians, he said, had actually fixed doses for each medicine, one, for example, never gave more than two grains of iodide of potash, even if it produced no effect. Others changed their prescriptions every few days and the patients thought they had tried everything, whereas they had in reality tried nothing. Thus, the drugs had not the slightest chance of benefiting the patient, as they were neither given in sufficient doses nor continued long enough.

Braid's work being practically forgotten, certain members of the Salpêtrière school revived many of the old errors of the mesmerists, and magnets, metals and medicines in sealed tubes, were once more supposed to be endowed with marvellous properties. These fallacies were for the second time exposed by the members of the Nancy School. They, like Braid in his earlier days, attributed the phenomena to emotional conditions excited in the brain of the patient. Everything was due to what they termed "suggestion." The phrase soon became a fashionable one, and was considered to explain not only the curative powers of hypnotism, but also many therapeutic results which were usually attributed to the action of drugs.

Thus, Hack Tuke, in speaking of Sir Andrew Clarke, said: "His favourite drugs were bi-carbonate of potash and a vegetable bitter, but neither drugs nor diet formed the central factor of his treatment, or explained its success. 'Suggestion' lay at the root of it all. The term, however, is too mild unless understood in the technical sense in which it has been employed in recent times. In short, Sir Andrew out-Bernheimed Bernheim; he was, in a word, the most successful hypnotist of his day."

According to Sir Samuel Wilks: "To sit down in one's chair daily and write on a piece of paper the name of some drug for every ailment without exception, which comes under our observation is, in the present state of medicine, an absurdity, and is simply a pandering to human weakness. I do not say that drugs are not useful in a moral sense, I am merely contending that the method is not scientific, as we usually apply this term. I know of no more successful practitioner than the late Sir William Gull, and his treatment was rational, but he did not credit any particular drug with the properties ascribed to it by the patient. His prescriptions very often consisted of nothing but coloured water." Sir Samuel describes a "sixpenny doctor" at a cheap dispensary, who saw on an average seventy patients each evening, and whose almost universal medicine was a mixture composed of sulphate of magnesia, burnt sugar, and infusion of quassia. The following were his directions for successful practice: "Always give medicines which produce appreciable effects; then, also, the mixture must taste like medicine, and if it have a bad smell the patient will be better satisfied."

Sir Samuel states that "changes in the pathological views of disease have caused the whole method of its treatment to be altered again and again, and that further chemical knowledge frequently shows that the drugs we employ do not possess the qualities that we have been in the habit of attributing to them."

Putting aside for the moment the question of the connection between hypnotism and faith-healing, we find Hack Tuke and Sir Samuel Wilks practically reproducing the views of Braid and Elliotson to the effect that in many instances drugs owe their supposed therapeutic value to the faith of the patient. In typical cases the supposed curative agent is stated to be either non-existent or inert, as, for example, in the "coloured water" of Sir William Gull and the magnets of Benedikt. The latter still holds that magnets possess extraordinary therapeutic powers, despite the fact that scientific investigation has shown them to be devoid of the properties he attributes to them, and that they would be equally powerful if composed of pieces of wood. His method of treatment is, in fact, a reproduction of Perkins' tractors already referred to.

I do not believe that the greater part of medical treatment merits Sir Samuel Wilks' description, but certainly some of it does. It is thus identical with present day faith-healing, as the curative effects are due to the patient's belief in what does not exist. Such methods of treatment have their practical drawbacks; as advancing knowledge is ever likely to rob them of their power. Harness' electropathic belts undoubtedly sometimes caused the disappearance of functional nervous disturbances; but, to my personal knowledge, these in some cases immediately reappeared after the Harness' exposure. Would Benedikt's magnets be still efficacious if all his patients knew they were really powerless? Would Sir William Gull have continued to be equally successful had Sir Samuel Wilks' description of his method of treatment been universally accepted? Would it not be better either to substitute "suggestion" alone for "coloured water" and magnets, or to employ instead of them remedial agents of undoubted value?

In order to bring hypnotism under the head of faith-healing, one must be able to show that the patient believes in the operator's power of healing, and that nothing beyond faith is involved. Since the days of Braid, both physician and patient have learnt that the curative power is due to changes in the patient's own nervous system, and is independent of any mysterious power possessed by the operator. Faith is not necessary for the induction of hypnosis. Some who believe they can be easily hypnotised prove refractory, while others who are intensely sceptical are influenced at the first attempt. Further, in self-hypnosis, the influence of the operator is entirely eliminated, and if cure be due to faith, it is to the patient's faith in himself. Again, hypnosis is not an imaginary condition; even X not only admits its existence, but also warns us of its dangers.

Later, Braid recognised the complex and varied nature of hypnotic phenomena, and that these could not be explained by faith, suggestion, or concentrated attention alone. Many later observers have arrived at identical conclusions. It is now recognised that in hypnosis the attention may be directed to many points at once, and that suggestion is simply the artifice by means of which the phenomena are evoked. Wide differences exist between the results of suggestion in emotional states and suggestion in hypnosis. Thus:—

(A) *Suggestion in Hypnosis.*

(1) Once hypnosis has been induced, a wide range of phenomena, both mental and physical, can be evoked at any time, and—with the consent of the subject—by anyone. A considerable number of phenomena can be simultaneously evoked in the same subject.

(2) One phenomenon can be immediately changed into its opposite, *e.g.*, muscular rigidity into paralysis, anæsthesia into hyperæsthesia, &c.

(3) Hypnotic phenomena can be terminated at will.

(4) The date of the appearance of a given phenomenon can be delayed, *i.e.*, it can be suggested during hypnosis that the phenomenon shall not appear till twelve months afterwards.

(5) The suggestion will invariably be responded to, subject to the two important limitations that it contains nothing in opposition to the patient's moral sense, and that it is not beyond the range of his hypnotic powers.

(6) Under the conditions just mentioned, the exact nature of the response can be predicted, *i.e.*, similar stimuli produce identical results.

(7) Patients, who readily respond to suggestions when hypnotised, are frequently the very subjects who have for years resisted suggestion in the normal condition, even when this has been associated with emotional states. For example, a patient who had long suffered from dipsomania received many and varied suggestions in the normal state. All these, however, produced no result; yet, after a few weeks' hypnotic treatment, the patient abandoned the alcoholic habit, and, although over ten years have passed since then, has not relapsed.

(8) Hypnotic suggestion tends to gain strength by repetition.

(B) *Suggestion by Means of Faith and other Emotional States.*

(1) The resultant phenomena are usually isolated ones, or, at all events, much more limited in number than those which can be simultaneously evoked in hypnotised subjects. Further, they cannot be produced by anyone. Thus, the subject who has been influenced by the touch of a king would probably be unresponsive to that of a peasant.

(2) One phenomenon cannot be immediately changed into its opposite, without an alteration in the emotional state which had produced it.

(3) Emotional phenomena cannot be terminated at will.

(4) The date of the appearance of the phenomena can rarely be delayed and fixed.

(5) The phenomena are evoked with less certainty than in hypnosis; an emotional state which will produce a physical effect in one subject will produce nothing in another.

(6) Identical emotional states do not always produce similar physical phenomena. On the contrary, opposite conditions are frequently evoked in different subjects by identical emotions, *e.g.*, fear will paralyse one, and excite violent muscular contractions in another.

(7) Patients who are unaffected by curative suggestions in the normal state readily respond to them when hypnotised.

(8) An emotional suggestion frequently loses strength by repetition, *i.e.*, a subject may readily come to disregard former fears.

While X's fallacies were long ago exploded by the Nancy school, its views, in their turn, are now being attacked. Concentration of attention and suggestion are no longer generally regarded as explanatory of the hypnotic state. Personally, I am acquainted with no theory which satisfactorily explains hypnotism as a whole. The subliminal consciousness theory of Myers certainly marks an important advance, and gives one a clearer conception of the mental and physical states involved in hypnotic phenomena. It does not satisfactorily explain, however, whence the hypnotic subject derives his powers, nor how suggestion evokes them. X's treatment of Myers' theory is scarcely a scientific one. In reference to hypnotism, X says: "Hypotheses as to its nature may be useful, but should be carefully based on known facts, and not complicated by dialectical subtleties, such as the 'subliminal consciousness.'" Here, it is to be noted, that while X does not adduce a single fact in support of his widely varying hypotheses as to the nature of hypnotism, he is ignorant of, or ignores, those on which the subliminal consciousness theory is based. The theory is not Myers' alone, though his is probably the clearest statement of it. Many writers in different countries have recorded observations on which it is founded. X's assertion would have carried more weight if he had, at the same time, given us the result of his examination of the experiments of Azam, Delbœuf, Pierre Janet, Max Dessoir, William James and others. It is to be noted that William James states that the principle upon which the subliminal consciousness theory depends is now largely admitted by science.

According to X, the assertion that it (hypnotism) unlocks or redevelops some latent organic endowment is beyond possible proof, and is opposed to all evidence of organic evolution. That the hypnotised person possesses powers over his organism, which are not shared by the ordinary individual, instead of being beyond possible proof, is now one of the commonplace facts of science. The ordinary individual cannot induce anæsthesia at will, nor can he select painful sensations from amongst a group of others and prevent these alone from reaching consciousness. To the deeply-hypnotised subject, however, this feat is an easy one, as I have frequently demonstrated to members of our profession.

X says: "We recall a visit to the Zurich Asylum, where Professor Forel has long studied the phenomena of hypnotism, and where many of his 'subjects' could be seen amongst the members of the staff. Only one patient, an habitual drunkard, was then sensitive to the hypnotic influence exerted by Professor Forel." As X in the next sentence states that he personally had only employed hypnotism in a few cases and with unfortunate results, those unacquainted with Forel's work would naturally conclude that Forel too, like X, had found hypnotism of little therapeutic value, and so abandoned it. This imputation is keenly resented by Forel. The following are extracts from two letters which he wrote to me from Chigny, in October and December, 1898. He said: "I have left Zurich as I found the work too much for me, but it is altogether false that I have given up hypnotism. On the contrary, I treat patients here by this method, and continue to get very good results. The *Journal of Mental Science* has stated a thing which is false. I have hypnotised over a thousand persons and have influenced about 95 per cent. The therapeutic results are excellent. The allusion in the *Journal of Mental Science* is a bad joke, and reminds me of the Englishman who in passing through France saw an ugly girl with red hair at a station and concluded that all French girls were ugly and had red hair. I have no recollection of the visit referred to, but if I then hypnotised an alcoholic that does not prove that I did not hypnotise 999 other persons. In any case, it is false to pretend that amongst the numerous patients I have hypnotised one alone was susceptible; probably this gentleman understands nothing about the subject."

Forel is the author of "Der Hypnotismus, seine psychophysiologische, medicinische, strafrechtliche Bedeutung, und seine Handhabung," which has already reached its third edition. Until recently he was the editor of the *Zeitschrift für Hypnotismus* and has contributed many articles on hypnotism to that and other medical journals. It was, in fact, owing to his researches that the great hypnotic movement spread from France to Germany.

X states that many of Forel's "subjects" could be seen among the members of the staff, but does not mention that they were hypnotised for physiological and psychological experiment. Forel found, for example, that he could produce redness of the skin and urticaria by suggestion, and also action of the bowels. He records several instances in which he succeeded in causing the appearance or disappearance of the menses during hypnosis, and others in which the same results were brought about by post-hypnotic suggestion.

In the *Zeitschrift für Hypnotismus*, for 1898, Dr. Inhelder, formerly Assistant Physician to Professor Forel, records the experiments made with hypnotised warders, both male and female, for ten years (1887-1897), in the night watching of dangerous lunatics. Hypnotised warders were trained to sleep by the bedside of dangerous patients and to awake the instant the patients attempted to get out of bed. Sounds which had no import with reference to the warder's duties were inhibited by suggestion. Warders in this way sometimes performed night duty for six months, and worked hard all day without showing signs of fatigue. Dr. Inhelder gives a detailed account of these cases and states that the results were uniformly successful. No accident of any kind occurred.

In reference to these experiments, Forel claims that they were entirely without risk, and were conducted in such a rigorously scientific manner as to exclude all possible sources of error.

When I visited Forel in 1892, he successfully repeated several of these experiments, and also showed me a number of patients who were undergoing hypnotic treatment.

The Therapeutic Value of Hypnotism.

In 1891, Forel published the following list of diseases, which, in his experience, responded best to hypnotic treatment: All forms of hysteria, including hystero-epilepsy, neurasthenia, nocturnal terrors of children, chorea, enuresis nocturnalis, stammering, insomnia, headache, neuralgia, sea-sickness, vomiting of pregnancy, psychical impotence, perverse sexual disturbances and bad habits of all kinds, alcoholism and morphinism, chlorosis, menstrual disorders, constipation, loss of appetite, nervous dyspepsia, chronic muscular and articular rheumatism.

This list, he said, was by no means complete, but would be sufficient for any fresh worker in the field of hypnotism to begin with.

Hysteria.—According to many authorities, hypnotic treatment gives the best results in—

(1) The convulsive attacks of *grande hystérie*, and in the symptoms which sometimes persist after these attacks (paralysis, contractures, spasms, anæsthesia, amoroses, &c.).

(2) Monosymptomatic hysteria (monoplegia, hysterical mutism, aphonia, hiccough, cough, blepharospasm, discromatopsy, &c.).

(3) The various manifestations of ordinary hysteria (insomnia, dyspepsia, visceral and menstrual troubles, neuralgia, &c.).

(4) Mental troubles of a hysterical nature (perversion of sentiment, obsessions, irresistible impulses, hallucinations, melancholia, maniacal excitement, &c.).

Bérillon states that for three years he watched the hypnotic treatment of *grande hystérie* by the late Dr. Dumontpallier at the Pitié Hospital. In the majority of cases, not only did the convulsive attacks disappear, but the other symptoms also. Some of these patients are now in excellent health, married and mothers of families, while others occupy important posts.

Dipsomania.—Florel claims to have obtained excellent and durable results in this disease, and there are few, if any, of those engaged in hypnotic work who are unable to report similar successes. Ladame draws special attention to three cases treated by Florel. All had had attacks of delirium tremens and were inmates of his asylum. They were extremely difficult to manage and expressed a determination to resume drinking as soon as they were liberated, but, despite this, complete recovery followed hypnotic treatment.

Vicious and degenerate children.—Bérillon and others assert that many carefully observed facts prove the therapeutic value of suggestion in the following diseases of children: Incontinence of urine and fæces, nervous "tics," nocturnal terrors, chorea, onanism, blepharospasm, &c.

Obsessions.—Hypnotic treatment has yielded brilliant results in various forms of obsession, and the following, amongst others, cite successful cases: Liébeault, Schrenck-Notzing, Hecker, Wetterstrand, de Jong, van Eeden, van Renterghen, Bernheim, Gorodichze, Voisin, Burot, Mavrokakis, Bourdon.

Neurasthenia.—Schrenck-Notzing records 228 cases treated by Brügelman, Bérillon, Bourdon, Voisin, Burckhardt, Forel, Ringier, Hecker, Ritzmann, Bourru and Burot, Stadelman, von Corval, Bernheim, van Renterghen, Wetterstrand, himself, and others. Of these, 31 per cent. were reported cured.

Menstrual disorders.—Successful cases of amenorrhœa, dysmenorrhœa, and menorrhagia are cited by Forel, Tyko Brünnberg, Delius, Wetterstrand, Voisin, Bérillon, Gascard, Journée, Maradon de Monthyel, Burot, Dècle, &c. Many of the cases were of long standing, and had resisted other methods of treatment, while their recovery is confirmed by later reports.

Insanity.—From 1880 till his death, in 1898, Voisin devoted himself largely to the treatment of mental disorders by hypnotic suggestion, and claimed to have cured many cases of undoubted insanity. The majority of the patients suffered from mania, or from melancholia with hallucinations, suicidal impulses, and delusions of persecution. Many of the cases are of extreme interest and carefully reported. The following is an example:—

T., aged 40. Suicidal melancholia with hallucinations. When the patient entered the asylum the skin round her neck was ecchymosed, the injury having been produced by a cord. Owing to her constant attempts at suicide it was necessary to put her in a straight-jacket. When she spoke, which was at rare intervals, she stated that she was accused of murder, and the police had come to arrest her. She rarely moved during the day, but at night was restless, and did not sleep. There was incontinence of urine and fæces. For fifteen days she had refused food. Complete recovery after a month's hypnotic treatment.

Dr. Répoud (Cantonal Asylum of Marsens, Fribourg) claims to have obtained results similar to those of Voisin in cases of insane patients who were not hysterical. Burckhardt (Préfargier Asylum) records successful cases of delusional insanity and acute puerperal mania; Liébeault, hereditary suicidal monomania; Dr. Brémaud (Brest), religious melancholia following confinement; Dr. Velander (Yonköping, Sweden), melancholia with mutism.

Dr. Robertson, while at Morningside Asylum, was able to hypnotise and control the worst case of suicidal and homicidal mania there had been in Morningside for ten years. He found hypnotism of much value in the management of violently insane patients.

In 1897, Dr. Woods, Hoxton House Asylum, reported good results in several cases of insanity and allied disorders.

Forel suggested that Voisin's so-called insane patients were not genuinely insane, and only suffered from aggravated forms of hysteria. Voisin denied this, but said that even if this were so, the successful treatment by suggestion of hysteria alone marked a therapeutic advance of no little importance. Our asylums, he said, contained a large number of hysterical insane who were violent and dangerous, and who inspired both disgust and pity by their tendency to drink and steal, and by their lies, dirtiness, and obscene and unnatural acts. Some of those who had long been asylum inmates were now, thanks to hypnotism, leading active and useful lives, a fact which he thought went far to prove the value of this form of treatment. Forel himself, at a later date, recorded a case of delusional insanity with hallucinations, which he had successfully treated.

Those unacquainted with hypnotic literature might be led by X's statements to conclude that hypnotism at home was represented by his failures and abroad by Forel's solitary dipsomaniac. The account I have just given, though the merest outline of hypnotic therapeutic work, is sufficient to indicate that X's picture of it is, to say the least, lacking in proportion and perspective.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At the Clinical Meeting to be held on March 2, 1899, at 8.30 p.m., in the Medical Society's Rooms, 11, Chandos Street, the following cases were shown:—

Dr. F. E. Batten.—*Unusual form of muscular atrophy in a boy aged 5½ years.*

J. B., aged 5½; learnt to walk at two years of age, but never walked properly. He very easily becomes fatigued.

Present Condition.—Poorly-developed child with wasted limbs, especially below the knees and the forearms; contraction of muscles, giving rise to flexion of the legs at the hip and knee-joint and to flexion of the arm at the elbow; walks on tip-toe with toes inverted; unable to rise from the floor into the standing position, but can get on to his knees; all movements capable of being performed; no hypertrophy of muscles; knee-jerks present.

Dr. T. D. Savill.—*A case of epileptiform seizures of (supposed) vaso-motor origin.*

Mary M., aged 61, had been subject all her life, on and off, to three symptoms—"faintings," "flushings," and "nose-bleedings"—chiefly in her youth, and latterly, seven months ago, when she had had much trouble, the nose-bleedings ceased, and were suddenly replaced by the occurrence of more severe faints; and two or three months ago the fainting attacks *gradually* became attended by movements of the limbs until they assumed all the characters of idiopathic epilepsy, occurring several times daily, in some degree. Epigastric aura (which might be absent) followed by unconsciousness. The attack might or might not be attended by movements of the limbs. In one seen by Dr. Savill the patient, who was standing, gave an inarticulate cry, which was followed by a long inspiration. She seized hold of the screen which was near her, shook it violently, walked backwards with eyes fixed till she came to the wall, articulating as she did so "ub-ub-ub-ub-ub." The lips became somewhat purple, the face rather pale, and the pupils dilated. Saliva ran out of the mouth, and she made smacking movements with her lips as though tasting something. The respiration was laboured and the attack ended by a long expiration or sigh. The patient was quite unconscious, but the whole seizure only lasted about sixty or seventy seconds. When the patient came round she expressed herself as feeling perfectly well, and there was no drowsiness. The heart was somewhat feeble, and probably both ventricles were somewhat dilated. A faint systolic apical murmur (? of dilatation) was heard when she first came to hospital, but had since disappeared. The other viscera and the urine are normal. It was suggested that this case appeared to support the theory of the vaso-motor origin of epilepsy, on account of the gradual transition of obviously vaso-motor phenomena into attacks which were to all intents and purposes idiopathic epilepsy, occurring for the first time in a woman aged 61.

Dr. H. A. Caley.—*Case with symptoms of syringomyelia with sudden increase followed by rapid diminution in intensity.*

History.—W. H., aged 30, bricklayer. Rheumatic fever twice. No history of syphilis. Symptoms said to date from severe fall twelve months ago. Difficulty of walking gradually developed, followed by progressive weakness with numbness of right hand and arm. Marked disposition to sleep, occasional headache and vomiting, but neither severe. On Jan. 7, 1899, he had a "fit," in which he suddenly fell down unconscious. There were movements of head from side to side, but no clonic movements of extremities, arms crossed on the chest, with right hand tightly clenched. When the fit was over it was found that he could not stand or move his arms, which appeared quite helpless. Next morning was able to walk with difficulty. After this fit the previous symptoms were much intensified—marked weakness of both arms, "claw-like hand," with inability to move fingers on right side, legs unsteady and stiff.

Condition on admission.—Jan. 14, 1899. Marked weakness of right hand, with conspicuous wasting of thenar and hypothenar muscles and of interossei, 3rd and 4th being most affected. *R. D.* in right opponens and abductor pollicis, hypothenar muscles and 4th interosseus. First three interossei acted to faradism, but response increasingly feeble on passing to ulnar side. Also weakness with some atrophy (but no electrical changes), of right serratus magnus and rhomboideus major. Scoliosis. Marked rigidity of legs with spastic gait. Sensation normal over lower extremities and trunk as high as 5th rib, above this tactile sensibility normal or slightly blunted, painful and thermal stimuli not recognised as such. This also applied to sides of neck, front of face, and upper extremities excepting a small area along inner side of left upper arm. Knee-jerks greatly exaggerated, foot clonus and rectus clonus. Sphincters unaffected. Treated with liq. hyd. perchlor. and pot. iodid.

Subsequent progress.—During the ensuing week decided improvement; could walk better, legs less rigid, more power in right hand and arm; sensation unchanged.

A week later thermo-anæsthesia and analgesia over the chest much less marked. One month after admission, *i.e.*, five weeks after the fit, marked improvement in all respects. Weakness of right hand and arm less, gait comparatively normal, myotatic irritability less, thermo-anæsthesia and analgesia only partial in degree and much less extensive, being limited to sides of neck, first intercostal space, and arms.

Dr. Wilfred Harris.—*Hæmatomyelia.*

History.—A. J. B., aged 26, cook. Three and a half years ago, whilst bathing in the sea, experienced sudden pain across shoulders and down arms, and immediately after complete paralysis of both arms. Walked home quarter of a mile, and in another half-hour became completely paraplegic. Legs completely paralysed for a fortnight, then gradual improvement. Left arm began to improve after six weeks, and right arm in three months. Power over sphincters partially regained after two months.

P.S.—Slight spastic gait, drags left foot. Knee-jerks +. Complete wasting of right serratus magnus, latissimus dorsi, triceps, and lower half of pectoral and of upper portion of left pectoral, and slight wasting of left thigh and calf. Slight lateral curvature of spine.

Marked analgesia and thermanæsthesia over whole body and limbs up to middle of neck. Tactile sensation almost perfect. Now often burns himself unconsciously. Slight sphincter trouble.

Dr. J. H. Bryant.—*Functional tremor closely simulating paralysis agitans, following typhoid fever.*

Male, aged 31. Engine-room artificer, R.N., suffering from tremor of fingers, hands, &c. He was quite well as far as his present complaint was concerned until convalescence from typhoid fever, for which he was admitted to a Hong-Kong hospital on July 2, 1898. About a month after being in the hospital he noticed shaking of his hands and legs. It was first detected in and always had been most marked in the fingers and thumb of the left hand. He had also noticed since his return that he got occasional hot flushes, and that he sweated a good deal at night. He had had electrical treatment for six weeks, and thought he was much better for it.

Present condition.—He has marked tremor of both hands, especially of the left. The thumb and index-finger are continually on the move. The tremor may be described as resembling the characteristic pill-rolling movement of paralysis agitans. When he raises himself from the supine position without using his arms he gets a rather violent tremor of the muscles of his body and limbs. There is no obvious loss of power in the hands or arms. His legs appear to be weaker than they should be. There is no loss of sensation. The knee-jerks are brisk. There is no ankle or patellar clonus. No atrophy of the muscles. No R. D. No oculo-motor paralysis. There is slight temporary oscillation of the eye-balls when they are moved in a lateral direction; he cannot keep his eyes fixed and looking to the left or right without a feeling of fatigue and strain.

Dr. STANSFIELD.—*Epileptic insanity associated with mastoid disease. Operation: Improvement of mental symptoms, and cessation of fits.*

S. H., aged 31, laundress, commenced to have a discharge from the right ear when twenty years of age. A year later she had her first fit. Epileptic fits continued at frequent intervals up to the date of the first operation, a period of nine years, during the last three months of which she had 154. For the latter half of the nine years she had grave mental symptoms. The discharge from the ear continued during this time, but was intermittent. On January 28, 1898, her mastoid cells were trephined. She had had no fit since the operation, but she had continual headache, sickness and vomiting, with puffiness and tenderness of the scalp to pressure over the right ear. Dean's operation was performed on April 12, 1898, and the parts thus exposed were explored. No signs of pus were found, but the operation was contemporaneous with the disappearance of the above symptoms. The grave mental symptoms passed off with the first operation, and the dementia, which was becoming pronounced, has gradually cleared. There had been no more fits.

Dr. H. H. TOOTH.—*A case of atrophy of the lower extremities of the peroneal family form.*

The patient, a male, aged 21, a painter, suffered at six years of age from weak ankles. This weakness progressed and resulted in the formation of pes cavus, which required tenotomy on several occasions. A year ago the hands became affected with atrophy of the intrinsic muscles, especially of the first and second dorsal interossei. The muscles of the thighs were wasted in their lower fourth, and those below the knees had almost disappeared, with loss of faradic irritability on electrical stimulation. There were five in the family besides the patient, who was the third child. Of these all except one were affected with some atrophy of the leg muscles with more or less marked pes cavus.

BRAIN.

PART II., 1899.

Original Articles and Clinical Cases.

THE CHOROID PLEXUSES OF THE LATERAL VENTRICLES OF THE BRAIN, THEIR HISTOLOGY, NORMAL AND PATHOLOGICAL, (IN RELATION SPECIALLY TO INSANITY).

BY JOHN WAINMAN FINDLAY, M.D., GLASGOW.

WHILE much work has been done of late on the normal and pathological histology of the membranes and vessels of the brain, there has been practically nothing written for the last quarter of a century on the choroid plexuses themselves, with the exception in 1886 of Albarran's "Sur la structure d'un renflement situé au niveau du bord libre des plexus choroïdes des ventricules lateraux." It was, therefore, suggested to me, while acting as pathologist to the Crichton Royal Institution, Dumfries, that a research into the normal histology of this structure could not fail to be both interesting and profitable; and that in all probability there were important alterations to be found in the plexuses of the insane, analogous to those changes, described by Robertson and others, in the vessels and tissue elements of the pia-arachnoid of the brain. How far this has been borne out, the conclusions arrived at in the course of the investigation must show. These conclusions, I may state, are based upon the microscopic study of the choroid plexuses in sixty-five cases. Six of these, from general hospital cases, were kindly supplied to me by Dr. Sutherland, of the Western Infirmary, Glasgow. Forty-nine of the plexuses from the insane were given me by Dr. W. Ford Robertson, Pathologist to the Laboratory of the Scottish Asylums, Edinburgh, to whom I am also indebted for much valuable help. The remainder were from cases examined by myself at the Crichton Royal Institution. For the study of the normal structure I also made preparations from several absolutely fresh choroid plexuses of the sheep, ox and calf. I desire to express my thanks to Dr. J. Rutherford for placing unlimited time at my disposal during the progress of this research, and generally facilitating the work in every way he could. My thanks are likewise due to Dr. James Finlayson, Honorary Librarian to the Faculty of Physicians and Surgeons, Glasgow, to whom I am much indebted for the assistance he gave me in obtaining references in literature to the subject under discussion.

NORMAL HISTOLOGY OF THE CHOROID PLEXUS.

It is generally accepted that the choroid plexus is formed of pia mater, while it is held that the velum interpositum is composed of two layers of pia mater, between which are contained arachnoidal tissue and blood vessels.[1]*

As the choroid plexuses are only fringes of the velum interpositum, one would expect to find arachnoidal tissue here also, but such is not described, the generally accepted view being that they are composed of pia mater alone.

Lately, however, W. F. Robertson and Middlemass[2] have formulated the doctrine that in the soft coverings of the brain two distinct membranes do not exist. They hold that there is essentially only one structure throughout, and therefore only one membrane, which they propose to call pia-arachnoid. By means of horizontal sections Robertson has demonstrated that the so-called sub-arachnoid spaces may be seen in miniature from immediately under the endothelial covering on the outer surface right down to the inner surface just external to the cortical tissues.

To my mind, after an examination of Dr. Robertson's sections, this contention of the oneness of structure of the pia mater and arachnoid has been proved, and it seems to me that the basis of the choroid plexus consists essentially of the same structure as the pia-arachnoid covering the surface of the brain, and likewise resembles a "spongy lymph sac."

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* The numbers refer to bibliography at end of paper.

The basis of the choroid plexus is delicate white fibrous tissue. The white fibres are gathered together into bundles or trabeculæ of varying thickness and length. These bundles interlace with and cross over one another, after the manner of a network, forming numerous spaces of all shapes. These spaces, inaccurately placed above and alongside of one another, form freely communicating cavities containing fluid, and are lined throughout by a single layer of flattened endothelial cells with large oval nuclei. The meshes of these networks are larger and smaller, the largest being quite microscopic in size, and the smallest showing only a solitary endothelial cell.

In the pia-arachnoid itself these spaces are largest in the centre of the membrane, where they form the so-called "subarachnoid spaces," or about the base of the brain the "arachnoid cisterns."

Much the same condition may be seen in the more central parts of the glomus—a fusiform swelling of the plexus seen at the junction of the body with the descending horn of the lateral ventricle—where these cavities often attain a considerable size. This might be taken as evidence that the choroid plexus consists of two distinct structures, viz., an external layer of pia mater and a central mass of arachnoidal tissue. Such, however, I cannot believe. It seems to me that, as in the case of the pia-arachnoid on the surface of the brain, there is only one structure throughout. Most marked in the centre of the glomus, the lymph spaces get smaller and smaller as we pass towards the surface, till it becomes difficult to make them out. But even here in many cases it is possible to do so, and at most these relatively dense portions of the plexus are but loose areolar tissue lying alongside distinct and easily recognised sinuses.

The choroid plexus, then, may be said to be composed of a duplication of the external pia-arachnoid, since the basis of the plexus resembles it in every way.

There is also a small quantity of elastic tissue in the form of fine threads or filaments. These elastic filaments may be seen lying longitudinally on the surface of a connective tissue bundle, and also winding round and encircling it with several spiral turns. This is brought out by treating a portion of teased choroid plexus with acetic acid. The connective tissue trabeculæ then swell up, and show circular or spiral markings with a distinct dark thread at the point of constriction. A continuous spiral may be traced here and there around the bundle, but the appearance of separate rings is more commonly observed.

This arrangement of the elastic fibres in areolar tissue was first pointed out by Henle: where only separate rings are observed, it has been suggested by Schäfer that this reaction is not due to the presence of elastic fibres, but that "the bundles in question are naturally invested with a delicate sheath, which, like elastic tissue, resists acetic acid, but, on the swelling up of the bundle under the operation of that agent, is rent into shreds or segments, mostly annular or spiral, which cause the constrictions. In other cases the union of branches of the cells around a bundle may be the cause of the appearance."[3]

Connective tissue cells are also found on the surface of the bundles or lying between them, and most frequently assume the spindle or branching form. Pigmented cells may here and there be seen, but their number is never large.

Vessels of the Choroid Plexus.

The choroid plexus is a very vascular structure and its vessels are exceedingly tortuous. The large choroidal vein and the principal arteries run longitudinally along its base. The branches of the latter pass mainly upwards and go on dividing till eventually a very close capillary network is formed.

Arteries.—The larger arteries contain several layers of muscular tissue, and a well marked adventitial coat composed of wavy connective tissue fibres running parallel to the course of the vessel. Outside this adventitial coat, and flattened along it, are the lymph spaces of the pia-arachnoid; indeed, the connective tissues of the two structures gradually merge into one another. The elastic lamina, too, seems to be well developed in these arteries.

Before describing the arterioles as normally met with in the choroid plexus, let me quote from W. F. Robertson's description of them as found in the pia-arachnoid of the brain:

"There is a fact regarding the arterioles of the pia-arachnoid that, I think, helps us to understand the true constitution of the membrane. It is that they have no proper adventitial coat. Immediately outside of the muscular wall there is a single layer of endothelium which is continued down to the capillaries as pointed out by Klein. Obersteiner believes that this layer forms the outer wall of a lymph sac, a point that must be regarded, I think, as doubtful. Beyond this endothelial layer lying on the muscular coat, the vessels, with the exception of some of the very largest of them, have no special investment of longitudinally disposed fibrous tissue, such as is found in the vessels elsewhere. They are, as it were, naked vessels surrounded by trabeculæ and lymph spaces. The trabecular tissue, however, practically forms for them a common adventitia. From a consideration of these features of structure Dr. Middlemass and I have advocated the view that the whole extra-vascular structure of the soft membranes may be looked upon as the conjoined and hypertrophied adventitial coats of the pial vessels, the lymphatic spaces of which have undergone a special development so as to form a spongy lymph sac."[4] More recently W. F. Robertson has altered his opinion as to the naked condition of the arterioles. He now holds that they are possessed of a delicate adventitial coat, and maintains that this additional observation is in no way out of harmony with the general spirit of the above doctrine.[5]

In many cases it is impossible to make out any adventitial layer; and immediately under the muscular coat appear round, oval, or spindle-shaped spaces of small size and lined by an endothelium. In other cases, again, a very thin layer of longitudinally disposed fibres of connective tissue may be seen, and I feel assured that an adventitial coat exists, though in places so thin as to be discerned only with difficulty or not at all. The presence, moreover, of such is further proved when, thickened by hyaline degeneration, the adventitia appears as a well-marked regular band beyond the muscular coat, even in arterioles with only one layer of muscular cells. Beyond the adventitia, now and then, appearances, as of a continuous layer of endothelial cells, may be made out, or a longitudinal channel lined by such cells seems to exist between two small arterioles. Such a condition, however, does not appear to me to imply the existence of a special lymph sheath, but is most probably produced by one of the spaces of the "spongy lymph sac," altered in shape to suit the exigencies of the case. Albarran[6] considers the vessels of the choroid plexus as destitute of a lymphatic sheath. Moreover, one can see no necessity for such if the contention of Middlemass and Robertson be correct—that "the whole pia-arachnoid may be looked upon as the conjoined and hypertrophied adventitial coats of the pial vessels, the lymphatic spaces of which have undergone a special development so as to form a spongy lymph sac."

The intima of the small arterioles is likewise very thin, the endothelium being separated from the muscular coat by a very delicate layer of tissue. W. F. Robertson[5] holds that the elastic coat has normally no existence in the small cerebral arterioles. I cannot, however, agree with this, and it seems to me that even the smallest arterioles possess a fine elastic lamina. Indeed, in the normal condition the intima consists of practically nothing else but endothelium and elastic lamina.

Capillaries—The capillary network is best marked at the surface of the plexus, immediately under the epithelium and in the villi, but may be traced throughout a great part of the plexus. The more central parts of the glomus, however, show no such network, and the tissues here are practically non-vascular. The capillaries are of large size and are likewise surrounded by the spaces of the pia-arachnoid, and in parts little more than two layers of endothelial cells—that of the capillary itself and that of the space—seem to separate the cavity of the lymph sinus from the interior of the capillary. There is no reason to believe that the minute "vasa serosa," described and figured by Luschka[7] in this structure, have any real existence.

The capillaries here, moreover, are remarkable for the fact that they possess a special adventitia in addition to their endothelial intima. There are two forms of nuclei in these capillaries, elongated, and rounded. The former belong to the intima, stain faintly and do not project from the capillary wall; the latter, on the other hand, are adventitial, stain deeply and do project. This adventitial investment must be considered as consisting of two elements, connective tissue cells and exceedingly delicate fibrils, the latter being continuous with the connective tissue of the adventitia of the larger vessels. These fibrils in the capillary walls are of great importance, for it is in them, as Woodhead[8] points out, that the process of waxy degeneration is supposed to occur. Small capillaries, too, may be normally seen immediately under the muscular coat of arteries and arterioles and quite close to the intima of veins.

Veins.—The veins are very numerous, and so frequent are their windings and bendings that there almost seems to be in the glomus an arrangement of blood sinuses approaching the character of cavernous tissue. In sections the blood spaces appear large and very irregular in shape, and though at first inclined to attribute these to the presence of a cavernous arrangement here, I am now convinced that numerous and very tortuous veins are all we have. The veins are lined by an endothelium and have remarkably thin walls, which are devoid of muscular tissue. The fibrous tissue of the walls very quickly merges into the surrounding spongy tissue, and spaces lined by an endothelium are seen quite close to the intima. Indeed, the wall of a vein might be said to be composed of only a more compact pia-arachnoid tissue.

Villi.

The surface of the choroid plexus is beset with a large number of highly vascular villous projections. These are of all sizes, and the largest may branch and subdivide many times before the ultimate villi are formed. Where the plexus does not present such a shaggy appearance to the naked eye, small non-branching villi may be seen closely arranged alongside one another.

Each larger villus has an afferent artery and efferent vein. These open into a capillary network lying near the surface, and in the ultimate villi a capillary loop, in the form of a bow, may be seen close under the epithelium, which everywhere covers the plexus. The same capillary may pass through more than one villus. The greater part of the villus structure consists of epithelium and capillary, the smaller remainder being made up of homogeneous connective tissue, with a few oval, spindle, or ramifying corpuscles. Occasionally, however, this tissue appears fibrillated, but only in the very largest villi can spaces and trabeculæ be made out, a loose areolar tissue being more commonly observed.

Epithelium of the Choroid Plexus.

The free surface of the villi and of the depressions between them is everywhere covered by an epithelium.

Hæckel[9] regards the epithelium as composed of a single layer of cells, but in pathological conditions he has seen these cells greatly increased in number. Heldt[10] likewise describes only a single layer of pavemented epithelium, and denies the existence of several layers. With Hæckel and Heldt may be classed Schäfer, Dejerine,[11] Koelliker,[12] and others.

Luschka,[7] on the contrary, has described this epithelium as approaching the stratified formation, recognising not only two or three layers of cells situated above one another, but also different developmental forms.

In many places it can be demonstrated that only a single layer is present, but then just as often three, four, or more layers may be seen, the two conditions lying alongside one another. Hæckel, we saw, regards the latter state as due to pathological proliferation of the epithelium. Such, however, I cannot believe. The existence of several layers of cells seems too common to be accounted for in this way, being found in all my cases in parts without exception, and also in the choroid plexuses of sheep, calves, and oxen examined. Beyond a doubt several layers of cells normally exist, and may be traced through their different stages of transition as we pass to the surface. Moreover, in a few human plexuses I have seen the deeper and more active cells in actual process of division, still further demonstrating, as Luschka held, that there are not only two or three layers of cells situated above one another, but also different developmental forms. Where only one layer of cells exists I must suppose that the others have been brushed off, though I have to admit that narrow spaces covered by, and apparently unable to contain more than, a single layer of epithelial cells are found. It is possible, however, that the contraction of the tissues, in process of hardening, has altered the character which such a space possessed during life. These epithelial cells form a transitional rather than a stratified variety of epithelium, for the outermost cells never show any tendency to become flattened.

The individual cells vary in size, ranging from a little less than ·01 to ·015 mm. They are irregularly rounded or polygonal in shape, and when an epithelial surface is seen on the flat, they present an appearance like a piece of mosaic work. They fit closely by means of delicate processes which interlock between neighbouring cells. Henle has described these processes—which he terms "prickly"—as locking into suitable cavities in adjacent cells like a wedge. In the deepest layer small and slender processes may be seen coming off from the base of a cell at the angles and penetrating into the sub-epithelial layer. This last fact was first pointed out by Henle, and is of considerable importance as tending to support the view that the epithelium of the choroid plexus is homologous with the ependymal epithelium, which has such processes even in adult life. There are no cilia on either the cells lining the plexuses or the ependyma of the ventricles, but such are generally believed to exist in embryonic life. The protoplasm of the epithelial cell is very granular and contains a large round nucleus, likewise granular, in which a nucleolus can occasionally be distinguished. In addition there is usually present a clear-yellowish, or even brownish-coloured, highly refractive globule, sometimes approaching the dimension of the nucleus itself, but as a rule only attaining to a third or less of that size. By means of an oil immersion lens it may be seen that the granular appearance of the protoplasm is in reality due to an immense number of small globules, which appear to be of the same nature as the large one. Where there are several layers of cells *in situ* it may be made out that this vacuolation increases steadily as we pass to the free surface, until cells are reached entirely transformed into globules and showing no nuclear staining. Beyond this, again, the cells discharge their contents by breaking up, sometimes leaving an empty cell membrane to indicate where they have been. Before the cell actually breaks up the globules may run together to form a single large sphere. In celloidin preparations, where the ventricular fluid has got entangled in the recesses of the plexus, numerous droplets, clear and pigmented, and in every way similar to those met with in the epithelial cells, may be seen lying free on the surface; while here and there these same droplets appear to be running together to form larger drops.

The single globule, so often seen in the protoplasm with ordinary powers, almost invaribly becomes darkened on being treated with osmic acid, while the granules also are blackened. This reaction has led Obersteiner[13] and others to regard them as being of a fatty nature, and it seems to me some relation to a fatty substance may be inferred. Haeckel[9] accounts for the presence of the pigment in the epithelial cells by accepting the same view and then supposing a "transformation from fat into pigment, as has been already demonstrated in the case of certain other pigment granules." But there is, to my mind, no reason why we should not accept the pigment colouring the globules—or even the pigmented granules occasionally found—as normal to the epithelial cells, especially in conjunction with the frequency of normal pigmentation in the elemental tissues of the brain and its coverings.

Nerves of the Choroid Plexus.

Purkinje[14] has described a retiform arrangement of fine nerve fibres in the pia mater. Koelliker[13] has found that these nerves always follow the course of the arteries, and though he has never recognised them in their endings, he has traced them into the substance of the brain along with small arterioles. He states, however, that no nerves are to be found in the vessel plexuses of the brain, though he mentions that Bochdalek has seen fine nerve twigs in the choroid plexus of the fourth ventricle, these twigs proceeding from the roots of many cranial nerves.

In 1873 Benedikt[15] likewise described nerves in the plexus of the fourth ventricle. "From the medulla oblongata and also from the large multipolar cells in the restiform body, a small strap-shaped nerve bundle goes out into the choroid plexus of the fourth ventricle. This bundle consists of doubly contoured fibres, which pass out into the vessels of the plexus for vaso-motor purposes. In gold preparations these nerves may be seen in the neighbourhood of the larger vessels, and in the region of the smaller ones they appear as a terminal network of nerve fibres. Fibres also went out to the epithelial cells, but nothing can be said about the endings of the nerves." In 1874 Benedikt[16] traced these fibres to the vagus nucleus.

Since a nerve plexus has been demonstrated in the pia mater and in the choroid plexus of the fourth ventricle, one would expect by analogy to find a similar condition in the choroid plexuses of the lateral ventricles, but such has not to my knowledge been described.

It may be seen, however, that medullated nerve fibres do exist in the plexuses of the lateral ventricles, though they are present in very small numbers. I have not been able to trace them for any distance, and can say nothing as to their relations and distribution but that they seem to lie in the deeper parts of the plexus and sometimes in the neighbourhood of vessels. Both in man and the calf these fibres were brought into view by W. F. Robertson's modification of Heller's method. It seems not at all improbable that, as in the plexus of the fourth ventricle, these are vaso-motor nerves destined for the blood vessels.

PATHOLOGY OF THE CHOROID PLEXUS.

The choroid plexus is liable to be affected by many pathological changes. Each individual tissue may be attacked, or the lesion may be more or less common to the entire plexus. "The tumours are chiefly of the mesoblastic or connective tissue type, but epithelial or carcinomatous growths are also met with." Among the former Ziegler describes the following: "Sarcoma, alveolar sarcoma, endothelioma, myxosarcoma, myxoma, angiosarcoma, angiomyxoma, angiomyxosarcoma, angioma and psammoma, while more rarely fibroma, lipoma, chondroma, and cystic fibroma are present." Secondary growths of every kind are found, and of animal parasites may be mentioned the echinococcus and cysticercus.[17] Cholesteomata are rarely seen in the human subject, but seem to be somewhat common in the horse, where they may attain an enormous size.[18]

I have not had an opportunity of examining any of the above-mentioned conditions, and will now proceed to describe those changes which I have met with in the course of my investigation.

(a) *Concentric Bodies.*

These structures are very common in the choroid plexus. I have found them in every human case examined. They are often present in enormous numbers, and Heldt[10] has regarded them as being in great part normal and physiological. They have been described under different names: brain sand, acervulus cerebri, concentric concretions, hyaline concentric bodies, &c., and much difference of opinion has existed as to their mode of origin and composition.

In none of the choroid plexuses from the sheep or ox was I fortunate to meet with any of these bodies, though in the calf I, on one occasion, found what I took to be early developmental forms. Luschka has observed them in rabbits, dogs, and horses.

Similar concentric bodies are found in all the membranes of the brain and spinal cord; and constitute the chief element in those tumours called psammomata.

The usual form of these bodies is round, and, as a rule, they are surrounded by a well-marked hyaline capsule, or even a capsule of fibrous tissue with long, thin, spindle-shaped cells. They are marked with numerous concentric rings, these markings varying in intensity and number in individual bodies. Though the most common, this is not the invariable shape, and many different forms may be produced from several spheres coming together. Thus we may have a dumb-bell or trefoil-shaped structure, the interior showing distinct concentric bodies with rings of their own, while beyond these the body is surrounded by a common stratification. Rod-shaped bodies are occasionally seen, but they are decidedly rare. Irregularly ramifying forms, as described by Luschka, Hæckel and Koelliker, I have never seen.

Heldt, as the result of his observations, states that all these bodies show a thoroughly round shape. He is, I think, in the main right. All of them—with the exception of the rare rod-like forms—show a thoroughly round shape, or a combination of several such shapes, resulting in a more or less irregular figure, but one, however, which can always be resolved into a collection of spheres. They likewise vary very much in size, and are found in the plexuses ranging from ·01 to ·15 mm. in diameter.

Apart from their concentric markings, these bodies are, as a rule, structureless, but now and then the forms of globes or spheres can be made out in their interiors, though in many cases nothing more than a few granules are seen. Hæckel, however, found as the nucleus of such bodies nucleated cells, fat and pigment granules, heaps of shrivelled blood corpuscles, and rarely corpora amylaceæ. It is often possible to make out cells swollen from hyaline degeneration in the centre of these concentric bodies, but their nuclei are never visible. I have, however, never seen any appearances suggesting that blood corpuscles or corpora amylaceæ might form the nuclei or beginnings in the development of the same (concentric bodies).

In eosine and hæmatoxylin preparations they usually take on a bright-red colour, though sometimes the centre is coloured blue, while the periphery alone shows the eosine staining. In the same body, moreover, the different concentric rings may take up the eosine with different degrees of avidity. Carmine stains these bodies deeply, though in picro-carmine preparations here and there yellow rings are observed inside the red body, while the very small bodies are alone stained by the picric acid. Van Gieson's stain colours them a bright red, due to the fuchsine present in it. In the same way the fuchsine in the Ehrlich-Biondi stain attacks the concentric bodies, making them stand out in a remarkable manner from the surrounding faint-red or green-coloured tissue. The hyaline droplets, which are found in abundance around the concentric bodies, and which represent a phase in the development of the latter, do not take on the red fuchsine staining, but stain a dirty-green colour with the methyl green. Weigert's fibrine stain occasionally colours these concentric bodies, along with the hyaline connective tissue trabeculæ, a deep-blue colour, while the surrounding tissue remains unstained. These formations have never shown in any of my cases a waxy reaction with methyl violet. Osmic acid distinctly darkens these structures, sometimes bringing out a granularity not before evident, or accentuating the concentric markings.

All the older writers, including Obersteiner, Haeckel, Luschka, and Heldt, describe these bodies as concretions composed of carbonate of lime and carbonate and phosphate of magnesium. Heldt, however, lays special emphasis on the fact that there are also hyaline concentric bodies, which have not yet become calcified, present in the choroid plexus.

Aqueous solutions of mineral acids and acetic acid have practically no action on these structures; but if strong hydrochloric acid be used, a brisk effervescence takes place in many cases. Other concentric bodies, however, give off no gas on being treated with hydrochloric acid.

After examining my sections, I am of opinion that these bodies are not merely deposited from the tissue fluids, as Virchow[50] and others think, but that here we have an active proliferative process followed by a degenerative one. It has been already mentioned that the pia-arachnoid is a spongy lymph sac, made up of trabeculæ lined with endothelial cells. To begin with, probably as the result of some chronic irritative process, a proliferation of the endothelial cells occurs, and these cells may be seen undergoing division by the process of karyokinesis. In eosine and hæmatoxylin preparations the following phases of degeneration may be traced subsequent to the proliferation. The cell plate first of all swells up and becomes homogeneous, staining a very faint blue, while the nucleus has an increased affinity for hæmatoxylin. Next the protoplasm of the cell becomes possessed of an increased attraction for eosine, and usually has a somewhat granular appearance. Then the eosine staining becomes fainter and less granular, and with an oil immersion lens it can be made out that the protoplasm has formed inside the cell very numerous hyaline globules which, at first separate, eventually run together. The nucleus now loses its affinity for hæmatoxylin, stains more faintly, and in part shows the eosine colouration. This progresses gradually, till finally the nucleus is altogether coloured with eosine, being darker than the hyaline cell-plate. Afterwards this distinction is lost, and nothing is seen but a homogeneous hyaline sphere staining faintly with eosine, and measuring in diameter ·01 to ·05 mm. One of these spheres may form a concentric body, and numbers of such with only one concentric mark—doubly contoured spheres—may be seen. As a rule, however, these spheres, probably of a semi-fluid consistence, coalesce to form the more usual concentric body In many cases the cells take up this position before degenerating, and in a space a regular whorl of cells is seen, in appearance like a "cell nest," or as Ziegler puts it, like the skins of an onion. All stages of degeneration may be met with in these, from the swollen cell with the dark-blue nucleus to the homogeneous hyaline sphere. Nor does it seem necessary that these hyaline spheres should form concentric bodies in the identical spaces in which they are developed. It appears not at all unlikely that they may be carried along in the lymph stream circulating through these spaces till arrested by some obstruction. Indeed, the position and arrangement of many suggest this. Behind such an obstruction other hyaline spheres will be constantly added, and the never-failing pressure applied from behind will be sufficient to weld them into a single large mass, while probably, as W. F. Robertson indicates, the concentric rings appear subsequently owing to shrinkage.

The fibrous capsule so frequently present is added later, after the manner in which nature encapsules all foreign bodies; and in all probability the fibrous tissue owes its origin to the still healthy endothelial cells. There is never any round-cell infiltration around these bodies, the cellular aggregations in their neighbourhood being endothelial in character. Nor is there any need of such a round-cell infiltration to explain the subsequent development of the connective or fibrous tissue capsule, as "the endothelial cells," according to Metchnikoff,[21] "are actively engaged in the formation of new connective tissue."

This proliferation and degeneration of the endothelial cells may occur anywhere throughout the plexus, but is most marked in the glomus, where, too, the normal trabecular arrangement of the pia-arachnoid can be most perfectly made out. In the same way cells may proliferate and degenerate, and concentric bodies may form in the spaces close to the vessel wall; but, so far as I can see, there is no special tendency to the occurrence of them here. When concentric bodies develop in spaces immediately outside a vessel, they may by pressure seriously obstruct it, or lead to the absorption of a hyaline adventitia. These facts probably account for the description of buddings or ampullary dilatations of the walls of the blood-vessels of the choroid plexus by Cornil and Ranvier,[19] and also for the further idea that the incrustation of these buds by lime salts formed the concentric bodies. Heldt came nearer the truth when, denying the presence of buds on the vessels, he attributed the formation of these bodies to a hyperplasia of the adventitia, consisting of connective tissue-cells and stratified molecular mass, and forming excrescences on the vessel wall. At no time, however, do these bodies develop in the adventitia, but always in the lymph spaces beyond.

While the above is the most common mode of development of concentric bodies, I do not think that it is the invariable one. When hyaline degeneration attacks the arteries and capillaries, these sometimes become converted into solid tubes. This condition, though in all likelihood happening often, is but rarely met with, suggesting the idea that some further change occurs in these solid hyaline vessels. These hyaline cylinders most likely split across, while the segments contract into the form of rounded masses, which later acquire concentric markings.

Very frequently, too, in the midst of concentric bodies, hyaline rings are met with containing degenerating cells in their interiors. It is impossible to resist the conclusion that these hyaline rings are developmental forms of concentric bodies. The hyaline circle is of varying size and thickness, and may show concentric markings with spindle-shaped cells between the different layers. The interior of such a ring may be lined or packed with cells, all more or less showing signs of breaking up, with diminution or loss of nuclear staining. It is difficult to trace the origin of such a condition, and the different appearances are most conflicting and confusing. In a few cases it has been possible to demonstrate that these are merely depressions from the surface epithelium—what may be termed acini in transverse section—somewhat similar figures in longitudinal section allowing the continuity of the epithelium to be traced. But this explanation does not satisfy for all. Thus, a small hyaline ring with a single degenerating cell in its interior could not represent a prolongation from the surface, and most probably is a hyaline capillary in transverse section with a contained endothelial cell. Others which are larger most likely represent small hyaline arterioles or venules, with degenerating endothelial cells in their interiors; and in a few cases this can be conclusively proved by the detection of blood corpuscles in the lumen of such a structure.

In conclusion, it may be stated that the majority of these concentric bodies are composed of hyaline material, this being more especially brought out by their reactions with eosine and fuchsine. But this hyaline material seems to be an exceedingly unstable substance, leading at times to considerable variations in staining. Thus is the fact explained that in eosine and hæmatoxylin preparations these bodies on occasions show a preference for the latter, and take up the former with different degrees of avidity. In the same way the reactions with Ehrlich-Biondi, and the occasional colouring with Weigert's fibrine stain, are accounted for. The conclusion, therefore, of Alzheimer[25] seems borne out "that the colloid substance"—in this case synonymous with hyaline—"in the tissues undergoes transpositions, and becomes altered in its reaction and chemical property." But these bodies are not all hyaline, as the effervescence with hydrochloric acid proves. Some of them are concretions, but they are decidedly in the minority, and are only met with in abundance in senile cases. In cutting tissues not previously decalcified, the simply hyaline bodies cut easily, and offer no resistance to the knife, while the concretions will not cut, and tear or break up the tissue. There is not much, however, in the microscopic appearances, apart from a more or less marked granularity in the latter, to distinguish between them. Both are alike, and the only reliable test is the chemical one with hydrochloric acid. Moreover, it seems not at all unlikely, from the reaction with osmic acid, that these hyaline concentric bodies preparatory to their calcification undergo a retrogressive fatty change, as so frequently happens in the case of calcifications elsewhere.

In my experience—which is also the experience of W. F. Robertson[28]—these bodies are never found in such profusion in the mentally sound as in the insane.

(*b*) *Mulberry Bodies.*

Closely allied to concentric bodies are structures which were first described by W. F. Robertson[23] in the dura mater under the name of "mulberry bodies." These bodies are also found in the choroid plexus. In comparison with the hyaline concentric bodies they are rare, but when present may occur in enormous numbers. They consist of groups of rounded or oval cells, which stain of a deep purple colour in hæmatoxylin and eosine preparations, and are perfectly homogeneous in appearance. The individual cells are pretty uniform in size, possessing a diameter of about ·01 mm. Each group may or may not be surrounded by a capsule. This capsule in some cases is only perceived with difficulty and, as a rule, is very faintly stained. Occasionally, however, it presents a deeper staining, and when this occurs the cells in the interior are more massed together, and discrimination between them is difficult. Mixed up with these mulberry bodies are isolated cells of the above description, which may or may not have a capsule, while all around are fully developed hyaline concentric bodies and pale hyaline spheres.

W. F. Robertson expresses no opinion as to the origin of these bodies, but I think I have traced the process by which they are produced.

Each little oval purple-coloured body represents a degenerated endothelial cell, and may be seen in process of formation in the spaces of the choroid plexus. It is likewise a hyaline degeneration of the endothelial cells, and this anomalous staining, as already seen, is no unusual feature of hyaline material. These little bodies, then, run together and form a mulberry-like mass, which later acquires a capsule. In all probability this capsule or envelope is elaborated not by these cells themselves, but is deposited around them from the fluid in which they are bathed. In their neighbourhood are seen large hyaline spheres, staining faintly, irregular in shape, and breaking down or gradually merging into the fluid about them. This capsule, at first indistinct, becomes more and more marked, till finally it assumes a very decided hyaline appearance around the mulberry mass. The oval bodies now begin to merge into one another and become less distinct. Then concentric rings appear in the middle of such a structure, and forms are seen with concentric markings in their interiors, and still surrounded by the oval purple-coloured cells. These likewise lose their identity and assist in the formation of a hyaline concentric body, which is the consummation aimed at.

I have gone somewhat fully into the development of these mulberry bodies and their further conversion into hyaline concentric bodies, because W. F. Robertson writes of them as though they were distinct entities. But such I have shown them not to be. They only represent another mode of expression of this hyaline change, which may occur under many different forms, and produce a material having very various staining reactions.

(c) *Cystic Degeneration of the Choroid Plexus.*

This is a very common condition, being found in a large proportion of cases. Indeed, so frequently are cysts present, that Faivre,[24] writing in 1855, described "choroid vesicles" as normal and peculiar to the human subject. It is interesting, on the other hand, to note that, as early as 1826, Robert Hooper, M.D., figured these cysts of the choroid plexus in his "Morbid Anatomy of the Human Brain (being illustrations of the most frequent and important organic diseases to which that viscus is liable)." Of my sixty-five cases examined, cysts were present in thirty-seven, while Ogston[25] only found them in 19 per cent. of the brains of known drunkards.

The glomus is pre-eminently the seat of this cystic degeneration, and cysts, though occurring, are never found to any extent in the other parts of the plexus. These cysts may be little larger than a pin's head, or may reach the size of a pea. In some cases they are few in number, in others they are very numerous, the whole glomus being converted into a cluster of cysts like a bunch of grapes in miniature. I have never seen them so large as a hazel nut, as Luschka describes, though the glomus itself may attain such dimensions. Cases are on record where cysts of the choroid plexus have reached an enormous size, distending the ventricles, pressing on the surrounding brain, and eventually causing death.[26] [27]

The walls of the cysts are thinner in some places and thicker in others, but everywhere delicate. They are very vascular, and numerous fine vessels may be seen coursing over the surface of the little bladders. The walls are further remarkable for the presence of a fine white dotting, due to concentric bodies embedded in them, or to small aggregations of cells filled with fatty granules. In one case a white patch, about half the size of a split pea, was seen at the apex of a cyst. On microscopic examination this was found to be composed of large cells filled with fatty granules, which were darkened on the addition of osmic acid.

The cysts have a smooth shining surface, and, as a rule, present no villi. As a result of the distortion caused by this swelling, vessel loops, attached by small mesenteries, are to be seen projecting from the surface of the glomus in greater numbers than they normally do.

The tissue of the walls is composed of a connective tissue stroma in which run numerous vessels, arterioles, venules and capillaries. This connective tissue forms in parts quite thick bands, which are produced by the obliteration of the normal spaces between the trabeculæ. The surface of the cyst, moreover, is very often destitute of an epithelial covering. Near the base of such a cyst the epithelium may be quite distinct, but as the apex is approached the cells become scattered, a bare patch showing up here and there, till finally a portion is reached where no epithelial cells can be seen. It is an open question as to how far such a condition is brought about artificially, and there can be no doubt that, in the handling of the tissues after death, the epithelium on the most exposed parts will be very liable to be rubbed off; still, from the frequency with which it occurs, I am inclined to the opinion that it is not altogether an "artefact."

The interior of the cyst is made up of a very open network of connective tissue trabeculæ, which are lined by degenerated and degenerating endothelial cells, scarcely one of which presents normal features. The spaces are filled with a thin fluid, in which float cells in different degrees of degeneration. Concentric bodies are of very frequent occurrence throughout the cyst, and may be found packed in the meshes over quite a considerable area. All around this looser and more open network, and gradually blending with it, is a dense tissue in which there has been very extensive proliferation of the endothelial cells lining the trabeculæ, and associated with this usually some thickening of the trabeculæ themselves. The proliferated cells, moreover, even in the quite dense portions, usually show early degenerative changes.

In the fluid which fills the cyst the following formed elements are suspended: (1) endothelial cells with an increase in the granularity of their protoplasm, the granules stained deeply with eosine, may or may not obscure the large oval nucleus; (2) cells showing one or more vacuoles in the protoplasm, with an occasional cell in which the nucleus is also vacuolated; (3) large globular cells whose contents consist almost entirely of a hyaline, perfectly homogeneous, and more or less opaque sphere, surrounded by a small circular or sickle-shaped zone of granular protoplasm, which contains a nucleus; (4) large homogeneous globules, in which the appearance of a cell wall may still be traced, but containing no other formed element; (5) still larger homogeneous hyaline spheres with no indication of cell membrane; (6) doubly contoured hyaline spheres, the inner sphere probably representing the transformed nucleus, the outer being derived from the cell protoplasm; (7) free nuclei, or nuclei with remnants of cell membrane and even protoplasm attached; (8) irregular masses of hyaline material; (9) extravasated and disintegrating blood corpuscles and granular *débris* derived therefrom; (10) hyaline concentric bodies of all sizes.

The above elements, with the exception of No. 9, arise from the endothelial cells lining the trabeculæ as the result of a degenerative process, and the following sequence of events may be traced. The endothelial cell first of all swells up, and the cell plate becomes coarsely granular, presenting in hæmatoxylin and eosine preparations numerous eosinophile granules. A vacuole now appears, encroaching more and more upon the protoplasm, till the granular contents of the latter are represented only by a circular or sickle-shaped mass at the edge of the cell. A nucleus may or may not be seen, and may appear to float in the vacuole, or remain attached to the cell wall embedded in the granular protoplasm. Then, very commonly the cell membrane ruptures and the contents are discharged into the lymph spaces, while in the fluid the free nuclei may be seen. The cell may, however, not rupture at this stage. The nucleus itself may become vacuolated and assist in the general distension of the cell, till nothing is seen but a homogeneous globule with a faint remnant of cell wall and protoplasm. In other cases the whole cell presents a coarsely granular appearance. These homogeneous globules thus produced may swell up still further till they rival the concentric bodies in size, and could the individual stages not be traced, one would be inclined to think with Alzheimer[22] that these large hyaline spheres are really elaborated from the tissue fluids, and not, as I believe, actually produced by cell degenerations. These large hyaline spheres may rupture, perhaps adding to the fluid contents of the cyst. More certainly, however, they run together, forming large irregular masses of hyaline material.

The connective tissue trabeculæ may become hypertrophied, and very frequently they undergo hyaline degeneration. And often owing to the pressure of the degenerated cells and fluid, these trabeculæ become broken down and absorbed, leading to the formation of spaces of large size, while, here and there, lying in the midst of hyaline spheres, may be seen free portions of the connective tissue trabeculæ.

The above are the microscopic appearances to be met with in the cysts of the choroid plexus, and as the result of my own observations I have arrived at the following conclusions as to their origin.

Hyaline concentric bodies are very commonly found in cysts, likewise the hyaline spheres, which have been shown to take part in the formation of concentric bodies. The degenerative process in the endothelial cells of the trabeculæ in cystic formation is very similar to that which precedes the development of concentric bodies. Indeed, so close is the resemblance that it is very questionable if we are entitled to discriminate between them. Still, to my mind, it is quite clear that cells break down into fluid in the cysts in a way that never occurs apart from them. But such degeneration of cells alone does not seem sufficient to account for the development of these cysts, though there is no doubt that the fluid found in them is in part due to this bursting of the endothelial cells affected with colloid or hyaline degeneration. In all the cysts I had an opportunity of examining the fluid was quite limpid. Colloid cysts, with gummy, viscid contents, have, however, been described by Wallmann[28] and Hoffmann.[29]

It seems more than probable that there are two processes here at work, a primary proliferation and degeneration of the endothelial cells, associated frequently with hyaline changes in the trabeculæ, and a secondary condition of œdema added thereto. Still, I do not think that Haeckel is accurate in saying that this solid structure—produced by proliferated cells and thickened trabeculæ—"may become through serous infiltration softer and more watery, and eventually form a bladder," for in my opinion the cyst is formed not in but behind this thickened mass. Moreover, he is wrong in attributing the cell formations to the connective tissue corpuscles.

Through the spaces constituting the pia-arachnoid, of which the choroid plexus is composed, there must be a constant circulation of lymph. This proliferation and degeneration of cells in many cases completely fills up these spaces, and a serious obstacle to the flow of lymph must result. As shown, too, when dealing with the formation of concentric bodies, hyaline spheres may travel till they stick in these spaces or channels, eventually blocking them up. Concentric bodies must have the same effect, and these are never present in any numbers without a concomitant development of cysts. There exist, then, very numerous points of obstruction behind which the lymph stream is constantly pressing. There is, in short, an obstructive œdema. The spaces of the pia-arachnoid become more and more distended with the lymphatic fluid, and larger spaces still are produced by the breaking down or absorption of intervening trabeculæ, while the cyst itself is produced by a number of such spaces lying adjacent to one another. The degenerated cells add to the fluid their quota, and where the tendency is for the cells to rupture in the manner described, then are the contents of the cyst colloid. In other cases, again, where the greater number of the degenerated cells goes to the formation of concentric bodies, the cystic fluid tends to be thin and limpid. Finally, such a collection of fluid may be shut off from surrounding parts by the occurrence behind the fluid accumulation of the same changes which led to the obstruction in front, and the frequency with which dense tissue is found all around the cyst seems to point to such a conclusion.

This is practically in harmony with Ziegler's idea that "the cysts of the pia mater would appear to depend on the presence of closed lymph spaces, congenital or acquired, in the pia mater or subarachnoid tissue," and in the case of the choroid plexus we see very distinctly how such closed lymph spaces may be produced.

So far as I can see, there is nothing in the position of these cysts to bear out the view of Luschka and Schnopfhagen,[30] that "they are due to the dropsical separation from one another of the two layers of the pia mater which constitute the tela and choroid plexus." Now and then a separation seems to occur, but can always be explained by the breaking down of trabeculæ and the joining together of numerous spaces to form a single large cavity.

No more can I agree with the opinion of Schrant and Förster,[31] that "the epithelial cells become converted into large and delicate albuminous cells, which then form colloid cysts." There is a constant change going on in the epithelial cells, and they normally undergo a process of vacuolation and rupture to form the choroid plexus secretion. With such factors at work one would expect *a priori* to find frequent examples of retention cysts. Appearances suggesting such are frequently seen both in man and the lower animals. But they never attain any size, and instead of actual retention cysts we may be seeing only the lower parts of the tubular depressions found between the villi, in the depths of which tubes secretion, though not actually held back, would be apt to lodge.

(*d*) *Thickening of the Trabeculæ, with Proliferation and Degeneration of the Endothelial Cells.*

I have described, first of all, the degenerations of the choroid plexuses leading to the formation of hyaline concentric bodies and cysts, as these are the most remarkable, but the endothelial cells and trabeculæ proliferate and degenerate to other ends.

"A milky and opaque condition of the pia-arachnoid is very common in the insane. In the majority of cases it is a well-developed state, and its absence is quite exceptional." (Robertson.)

Similar conditions are found in the choroid plexus, and are likewise very common. These changes are always more marked in the glomus, where the trabecular arrangement is on a larger scale and unequivocal.

Hyperplasia and Hyaline Degeneration of the Fibrous Tissue Trabeculæ.—The fibrous tissue trabeculæ undergo a slow hyperplasia, and are found in all conditions. In some cases the thickening is slight, the fibres being little more than swollen. In others, again, there is a distinct connective tissue overgrowth, and localised areas of dense fibrous tissue are produced, in which the normal pia-arachnoid spaces are obliterated or merely represented by endothelial cells. These altered and new formed fibres are very prone to undergo hyaline degeneration, and much thickened strands staining very brightly with eosine, and even large hyaline masses, may thus result.

Osteoid Plates.—On three occasions I found small osteoid *plaques*, distinctly laminated, and penetrated by well marked Haversian canals carrying blood vessels and numerous cells. In none of them was there any deposition of calcareous salts.

Hyaline Degeneration of the Connective Tissue in the Smaller Villi.—Before leaving the connective tissue alterations it will be convenient to describe hyaline degeneration of this structure in the smaller villi. Here, as already mentioned, the connective tissue is represented by a homogeneous matrix with very few cells: no trabeculæ or spaces can be made out. Now and then the tissue is fibrillated, while very occasionally distinct connective tissue fibres are seen.

Hyaline degeneration frequently occurs in this homogeneous connective tissue. The substance between the epithelium and the capillary loop swells up, acquires a more dense appearance, and stains very deeply with eosine. This increase of tissue finds room for itself by encroaching on the lumen of the capillary, which may eventually become obliterated altogether, leaving no trace behind it. Very often associated with this condition is a similar change in the capillary itself; and obstruction of the little vessel may really be brought about by a process of thrombosis. But soon this appearance of thrombus is lost, the clot becomes converted into hyaline material, and may even take part in the formation of a concentric body. When the villus becomes throughout hyaline and is robbed of its blood supply, the epithelium is almost invariably found shed. This desquamation, moreover, may occur while the capillary loop is still present, the intervening hyaline mass cutting off the source of nourishment from the epithelium. Villi over large tracts are found bared of their epithelium, and though at first enlarged, they eventually become much shrunken and distorted. This is a very common condition in senile insanity, and I would make the suggestion that, when spread over a large area, it may account for the atrophy of this organ so frequently seen in these cases.

Proliferation of the Endothelial Cells.—Associated with this change in the fibres there is proliferation—and degeneration—of the endothelial cells. When the thickening of the connective tissue trabeculæ is extreme, the changes in the endothelial cells are slight, or may be entirely absent. The endothelium is very commonly found shed in cases where the connective tissue fibres are thickened and the arrangement of spaces maintained. The proliferated cells frequently form dense masses in the spaces of the choroid plexus. This is not a round-cell infiltration, but is caused directly by a multiplication of the endothelial cells lining the trabeculæ. These endothelial cells may rarely be seen in actual process of division, and though often the nuclei in these cellular collections are rounder and smaller than those of the ordinary endothelial cells, it can be made out that in the main they resemble the endothelial type.

In connection with this condition occurring in the arachnoid in certain mental disorders Ziegler states that it is still doubtful whether these "milky thickenings" are always of inflammatory origin. "They are histologically due to fibrous thickening, endothelial hyperplasia, or more rarely to cellular infiltration." In the pia mater itself, he holds that these changes, in their later stages at least, are unmistakably inflammatory and accompanied by accumulations of leucocytes, especially around the vessels.

W. F. Robertson,[4] on the other hand, is very definite as to these aggregations being composed of endothelial cells entirely, and is of opinion that areas of small round-cell infiltration upon the vessel walls or elsewhere seldom occur. "It is only," he adds, "in advanced general paralysis, in syphilitic insanity, and in the very rare and still obscure condition known as purulent infiltration of the pia-arachnoid, that such an aggregation of round cells is added to the other appearances."

I cannot but favour the view of these collections of cells being endothelial in character, and though two syphilitic and seven general paralytic cases were examined, only in one of the latter was I able to detect round cells upon the vessel walls and in the midst of the endothelial proliferations.

Degenerative Changes in Endothelial Cells.—These proliferated endothelial cells by and by undergo degenerative changes, and these same changes may be observed without any previous cell multiplication.

(*a*) A very common degenerative process consists in the endothelial cells simply breaking down into granular *débris*, and spaces are frequently seen crammed with such material.

(*b*) Fatty changes are likewise often observed, and may be present over considerable areas. This condition is shown by the presence in the cell plate of numerous bright and highly refractive little globules or granules, which are darkened by osmic acid. Sometimes a nucleus can be distinguished amidst these fatty granules, in other cases it is impossible to do so. Cells thus affected may attain very considerable dimensions, a diameter of ·025 mm. not being at all uncommon.

Haeckel describes this as not a rare condition, "especially in association with the proliferating cystoid metamorphosis and hypertrophy of the connective tissue."

I am of the like mind, but feel convinced that he is wrong in saying that this fatty change occurs in the connective tissue corpuscles.

W. F. Robertson[4] and Adler have expressed the opinion that fatty changes do not take place to any great extent in this milky condition of the pia-arachnoid, but an opposite opinion is held by Ziegler.

Whatever may be the actual state of matters in the pia-arachnoid, I feel assured that these conditions met with in the choroid plexuses, and fairly comparable to the milky opacities of the pia-arachnoid, are associated with distinct fatty changes in the endothelial cells, often of a widespread character.

(*c*) Only on one occasion have I seen an example of what W. F. Robertson[23] calls "vitreous degeneration." This author has described the condition as affecting the endothelium on the surface of the dura and lining the perivascular canals of its substance. "This retrograde change," he adds, "though common and important in the dura mater, is somewhat rare in the pia-arachnoid."

In the early stages there may be vacuolation of the cell plate, but the change is essentially in the nucleus, which swells up and becomes vacuolated. These vacuoles, at first small and few, gradually increase in size and number, and run together, converting the nucleus into a collection of irregular cavities, staining faintly with hæmatoxylin. These vacuoles are, to begin with, separated by thin strands of granular protoplasm, staining more deeply with hæmatoxylin. Eventually, however, even these filaments disappear, and a large distorted form results, of a homogeneous glassy appearance, and staining very faintly with hæmatoxylin. This vitreous degeneration is altogether different from the hyaline change which occurs in these same cells. In the first place, it is principally nuclear, and, secondly, the homogeneous substance produced does not stain with eosine. It is, moreover, not a fatty condition, as osmic acid causes no blackening of the vacuoles or the completed homogeneous mass.

(*d*) Pigmentary degeneration of the endothelial cells is by no means a rare condition. It consists in an infiltration of the cell plate by numerous little globules of a bright yellow colour. The pigment, at first small in quantity, is gradually added to until no unaltered protoplasm remains, and in this way a very considerable increase in the size of the cell may result. This is undoubtedly a morbid change, as evidenced by the fact that almost every cell in a considerable area may be pigmented. Normally cells with pigment do exist, but they are always few in number and far between. It is, however, highly probable, as Robertson[4] suggests for this degenerative process in the pia-arachnoid, that "at the same time it is a change that may have a physiological basis in the normal pigment cells, just as in pigmentary degeneration of nerve cells the granules that replace the protoplasm are merely an increase in a normal element."

Foreign Elements in the Spaces of the Choroid Plexus.—Before passing on to a consideration of the changes in the vessels, it will be convenient to describe here some foreign elements commonly found in the spaces of the choroid plexus.

(*a*) Red blood corpuscles and granular *débris* resulting from their disintegration are frequently found. The occurrence of the former is, I feel sure, not altogether unartificial, for extravasated blood cells are more frequently met with in preparations which were frozen in dextrine and cut than in those firmly embedded in celloidin.

(*b*) Hæmatoidin granules are often present, especially in cases of senile insanity. They are always discovered around vessels, in the spaces just beyond the adventitia. The arteriole surrounded by them may be thickened or even occluded, and their occurrence must indicate a rupture near at hand in the course of the vessel. This pigment is of a dark coppery or old-gold colour, and, moreover, is almost never diffuse, but usually is found in little heaps or aggregations.

I cannot help thinking that these two conditions, viz., pigmentary degeneration of the endothelial cells and the occurrence of hæmatoidin granules, are closely related to one another. They are frequently associated, and while pigmentary degeneration may occur in the other insanities, it is specially common in that known as senile.

The endothelial cells throughout the body are remarkable for their active phagocytic properties, and on several occasions they were observed playing such a *rôle* in the spaces around a vessel. As a rule the hæmatoidin granules are darker in colour than the pigment found in the interior of degenerated cells. But to this rule there are numerous exceptions, and in many cases it is difficult to say whether we are dealing with hæmatoidin granules or cell pigment. From these facts, then, I think we are warranted in concluding that, in senile insanity at least, a great part of the apparent pigmentary degeneration is due to the endothelial cells having englobed these hæmatoidin granules, and in some cases further altered them. That the two pigments are identical with, or closely related to, one another and the blood pigment itself, receives confirmation from photography. Blood offers considerable resistance to the actinic rays, and in the photographic negative is represented by thin, clear areas. The same occurs when hæmatoidin granules or pigmented cells are photographed.

(e) *Hyaline-fibroid Change in the Vessels.*

This pathological alteration may be found in all the vessels—arteries, capillaries, and veins, but seems to affect mainly the two former. Of the arteries, the smaller ones and the arterioles show this degeneration to the greatest extent. The adventitia alone, or the intima and media together, may be affected, but by far the most common condition is to find the whole three coats involved.

Hyaline Degeneration of the Adventitia.—This consists in a homogeneous thickening of the longitudinally running fibrous tissue. The swelling may be slight or considerable, stains a faint pink with eosine, and as a rule is devoid of granularity. In the smallest arterioles, with only one layer of muscular cells, and in which the adventitia in the normal condition is made out with difficulty and appears as little more than a fine line, the diseased adventitia may form a swelling two or three times the thickness of the original wall. Where two arterioles with thickened adventitiæ lie alongside one another, it may still be possible to make out the presence of a lymph space between them lined with elongated endothelial cells. In other cases, however, where the swelling has been more considerable, this space becomes quite obliterated by the blending of the two adventitiæ, while here and there an elongated cell shows up to indicate where a channel or sinus has been. This thickening is often irregular, and frequently leads to considerable distortions of the vessels. When the hyaline swelling is regular there is very little alteration in the calibre of the vessel, but irregular and nodular swellings invariably lead to serious narrowing of the vessel tubes. The adventitia never becomes much thickened without the muscular coat showing similar degenerative changes.

Hyaline Degeneration of the Muscular Coat.—The muscular coat, as a rule, is only involved secondarily to a hyaline degeneration of the intima, the explanation of this being that the media derives its nourishment from the interior of the vessel, and not from without as in the case of the adventitia. This sequence of events may be traced very frequently, though now and then the media appears to degenerate without any previous hyaline thickening of the intima. In such cases, however, it is frequently found that, in the adjoining parts of the same vessel or in neighbouring vessels, the intima is thickened and hyaline. Probably in all cases of hyaline degeneration of the media, there is first of all a similar change in the intima. In cases where such a change cannot be demonstrated, we are warranted in assuming the presence of a chemical alteration in the constitution of the connective tissue fibres. Such chemical change in all probability precedes the more evident structural one, and this is all that is required to interfere with the normal process of osmosis. A chemical barrier of hyaline structure is interposed between the media and its nutritive supply, and thus is brought about a starvation of the muscular fibres leading to a subsequent degeneration.

The degeneration consists, firstly, in a swelling up of the muscular fibres, and in eosine and hæmatoxylin preparations the nucleus is well stained and is surrounded by clear protoplasm with no affinity for eosine. Then the nucleus gradually loses its tendency to stain deeply with hæmatoxylin, while the muscular protoplasm shows an increased affinity for eosine. Frequently, instead of this homogeneous layer, a finely granular appearance is produced from the presence of numerous eosinophile granules in the muscle cell-plates, and this may occur before total disappearance of the nucleus. In osmic acid preparations, it is found that some of these granules are of a fatty nature, for they become distinctly darkened by this reagent.

Hyaline Degeneration of the Intima.—The intima appears normally in the arterioles, when cut longitudinally, as a thin band of tissue covered by endothelium, between the lumen of the vessel and the muscular layer; while close to the latter can be made out, even in the smallest arterioles, a delicate elastic lamina.

The intima rarely becomes so much thickened as the adventitia. Such thickening, when it occurs, consists of a homogeneous hyaline mass, which is very irregular on its external surface, dipping down into the degenerated muscular layer, and pushing the elastic lamina before it. In no case, so far as I have seen, does the elastic lamina itself undergo this hyaline change. When present, it continues to separate the intima from the media, dipping down into the latter, and forming in it numerous loops in order to fulfil its purpose. Wherever the elastic lamina projects into the media, no muscle cells can be seen, though between the loops the muscle may retain its affinity for nuclear stain, and therefore its vitality. Into places where the muscle appears healthy, the elastic lamina and thickened intima have made no inroads. Therefore it may be assumed that the presence of points of diminished resistance has something to do with the excursions of the elastic layer.

In the intima this hyaline tissue may be invaded by cells and be converted into fibrous tissue, so as to present all the appearances of an endarteritis obliterans. In some cases the cellular infiltration is very abundant, while in others, again, remarkably few cells are seen, only an odd one here and there showing up between the thick fibrous tissue fibres. When the hyaline material has been replaced by new-formed fibrous tissue, the arterioles show a narrowed and irregular lumen. This narrowing and distortion in some cases is extreme, and actual occlusion may be brought about. The latter condition is, however, sometimes due to thrombosis occurring in the altered vessel, and the thrombus itself eventually acquires a homogeneous hyaline appearance. Lining the wall of such an endarteritic vessel, a single layer of endothelial cells is found next the lumen, and between this and a more or less degenerated muscular coat is a certain amount of fibrous tissue, with round, oval, or spindle cells between the fibres. The endothelium is frequently raised up from the thickened intima, leaving a space which contains no formed elements. Such a separation may also occur between a thickened intima and degenerated muscular coat, and likewise between a diseased media and adventitia. W. F. Robertson[6] thinks that these spaces are not altogether artificial, though perhaps exaggerated by bichromate hardening. They are filled with a clear fluid in which Robertson has occasionally seen a few leucocytes.

Mixed up with this fibrous tissue, especially when the thickening of the intima is considerable, may be seen elastic fibres or bundles. In transverse or longitudinal sections it is possible to make out two, three, or more elastic laminæ, separated by fibrous tissue and cells. In other cases it looks almost as though the entire thickening was due to a hypertrophy of the elastic lamina, with only a few cellular elements separating the different layers. The wavy course of the elastic lamina becomes still more wavy and, so far as I can see, shows no tendency to become straightened out, as Carl V. Rad[32] has found it in syphilitic endarteritis. It is often possible to make out that the different layers of elastic tissue become continuous with one another, forming eventually, mayhap only at one spot, the single normal elastic lamina. The secondary laminæ present the same exaggerated sinuosity of the original one, but are thinner, though by no means invariably so.

The elastic lamina is described by Schäfer as formed of elastic tissue, which occurs in longitudinal networks of fibres, consisting of one or more layers of different degrees of closeness. Under normal conditions, in any of the arteries in the choroid plexus, the elastic lamina appears as if composed of a single layer of elastic tissue; this layer varying in thickness with that of the artery. Still, it may be possible that, even here, the elastic lamina is made up of two or three layers, though such cannot be demonstrated. That the extra elastic laminæ owe their origin to a bursting asunder of these layers by new-formed tissue, as held by Carl V. Rad and Rumpf,[33] seems not at all unlikely. Thus, two elastic laminæ are explained by the division of the primary layer, and three by a further division of the secondary lamina, and so on. But it seems to me that the process, though perhaps in part, is not altogether a mechanical one, for there is no doubt that in many cases the elastic lamina is very distinctly hypertrophied. It becomes thickened and lengthened, so that its normal sinuosity is much increased. This great sinuosity, moreover, is not produced after death, for there is no associated distortion of the intima or endothelium. If the elastic lamina did not play an active *rôle*, the thickened intima would tend to obliterate the normal winding, making it in parts quite straight, as Carl V. Rad describes in the basilar arteries of the brain. Such, however, is not the case as found in the smaller vessels of the choroid plexus. Moreover, this view of Rumpf and Carl V. Rad does not explain the fact that in some cases the new-formed elastic lamina lies immediately under the endothelium.

In reference to this condition Heubner[34] advances quite a different explanation: "when the endothelium is no longer caused to proliferate cells from syphilitic irritation, its normal function begins, which it possessed at the time when the artery became thickened; it forms a fenestrated membrane over the new-formed tissue, as it formed the same in young organisms over the muscular layer." This further explanation of Heubner has more lately been supported by Löwenfeld,[35] and appears to me to be in accordance with the facts. Frequently, as already mentioned, a layer of elastic tissue may be seen immediately under the endothelium, and separated a considerable distance by new-formed tissue from the original elastic lamina. Moreover, though sometimes the continuity of this superficial layer with the deeper one can be made out, in other cases no such connection can be traced. The only way to account for its presence, then, is to assume, as Heubner does, that the endothelial cells may again become possessed of that power of forming elastic tissue which they had in the embryo. Though Heubner is only writing of syphilitic disease of the vessels, there is no reason why we should not apply his arguments to the vessel change under consideration, more especially in the light of the opinion expressed by him in this same work, that "there are no certain histological criteria for deciding on the presence of syphilis." The above views of Heubner and Carl V. Rad, while explaining the increase of the elastic tissue in some, do not do so in all cases. There occurs now and then a very distinct hypertrophy of the fenestrated membrane with little or no proliferation of the endothelial cells, and Löwenfeld describes one such case. From a consideration of these facts, then, I am forced to the conclusion that there must be some inherent vitality in the elastic lamina itself, and that under certain circumstances it is capable of proliferation and growth. At the same time this hypertrophy of the elastic lamina is not invariably associated with the hyaline-fibroid change. The fenestrated membrane may be broken through in parts or even be absent altogether.

Dilatations and Aneurisms of the Arterioles.—Narrowing and even occlusion of an artery or arteriole, as shown already, may be brought about by the hyaline change itself or by the subsequent reparative processes added thereto. But this is not the only alteration that may result. Sacculations and dilatations of the vessels, and even miliary aneurisms may occur; and, without doubt, are closely related to and dependent on hyaline degeneration in the vessel coats. This condition of dilatation has been called by Löwenfeld "die Rosenkranzform des Muscularisrohres," from the resemblance of the affected vessel to a rosary, and is found chiefly in the smaller arterioles. In such an arteriole there is throughout a mild degree of degeneration and hyaline thickening of the intima, and this, though slight, is sufficient to interfere with the nutrition of the muscular layer, as shown by the loss of nuclear staining and the presence of eosinophile granules in the muscle protoplasm. Where this degeneration of the media is most marked the vessel yields to the pressure of the blood, leading to the formation of a little fusiform dilatation, and the presence of several of these dilatations gives the appearance of a rosary. Moreover, in those places where sacculation has occurred, it may be seen that the thickening of the adventitia —almost invariably hyaline—is less marked, while at the points where the vessel presents a normal or narrowed calibre this thickening is more extreme. In other cases a nodular swelling of the adventitia may produce a localised fusiform thickening of the vessel, and such may be mistaken for a dilatation or an aneurism. But with this condition there is no increase in the size of the lumen; in fact, a narrowing as a rule occurs. These are evidently what Kromayer[36] has described as "pseudo-aneurisms."

On reviewing the pathological appearances of this hyaline-fibroid change, we may conclude that the greater the amount of hyaline material formed in the intima, the greater is the degeneration of the muscular coat, and the liability to dilatation. On the other hand, however, the facts show that the liability to dilatation is not in direct ratio to the hyaline thickening. Such hyaline material may become so thick and dense—this result may be attained by the transformation of the hyaline into fibrous tissue—as to compensate for the loss of the muscular coat, and prevent the occurrence of dilatation. This thickening, when carried beyond a certain point, leads to narrowing and even occlusion of the vessels; in other cases, again, pseudo-aneurisms are formed. A very large proportion of the cases examined showed evidence of chronic Bright's disease, and the increased blood pressure in this condition must have been an important factor in the production of dilatations.

While the small fusiform sacculation is the type of dilatation more commonly present, distinct miliary aneurisms, similar to those met with in the meninges, are found. In the meninges this condition most frequently exists in senile cases, and was found present by W. F. Robertson in five out of twenty-five such cases examined. I only, however, came across about half that number in the choroid plexus.

These aneurisms usually occur in the small arterioles with only a single layer of muscular cells, and are microscopic in size. The greater part of the aneurismal wall is composed of a dense layer of fibrous tissue, which is continuous with the hyaline media and thickened intima of the arteriole entering and leaving it. Scattered through this thick fibrous tissue are a few cells round and spindle-shaped, but nothing is seen to suggest the presence of muscular tissue. The inner surface of the sac is lined by a layer of endothelium. The "Rosenkranzform" dilatation must be considered as a step in the formation of a miliary aneurism, and rosary like arterioles are always present when an aneurism is found. Following on this the development of such an aneurism must have been gradual, allowing sufficient time for a reparative process to take place in its wall. This would be brought about, first of all, by the proliferated endothelial cells invading the hyaline mass, till a condition of endarteritis would be produced. But the growth of the aneurism would not be arrested here. So long as the tissue was incompletely formed dilatation would go on, and would only cease with the complete conversion of the granulation into fibrous tissue. These miliary aneurisms are true aneurisms, and not merely, as Eppinger[37] holds, examples of ectasis or dilatation in which all the coats of the vessel are present.

Charcot and Bouchard[38] say that "miliary aneurisms are the result of a diffuse periarteritis, the first stage of which is characterised by a multiplication of nuclei in the outer coat of the vessel. This inflammatory condition causes atrophy of the muscular layer, and so renders the vessel wall liable to yield to the blood pressure. In the later stages the excess of nuclei disappear, and the vessel becomes thickened and fibrous. It is in the early stage alone that it tends to dilate."

Robertson and Löwenfeld are of opinion that this view of Charcot and Bouchard cannot be borne out. No more can I agree with it, for around the "rosary form" of artery—undoubtedly the precursor of the miliary aneurism—there is always a complete absence of periarteritis.

So far as my experience goes, vascularisation of either the hyaline or fibrous thickenings does not occur to any extent. Newly formed capillaries are not infrequently found in the thickened adventitia, but never have I seen new-formed vessels in the thickened intima of the arteries and arterioles found in the choroid plexus.

Such narrowing and obstruction of vessels always lead to the compensatory formation of new vessels or capillaries, and such in all probability exist here. But on this point one cannot dogmatise, for the vessels of the plexus are everywhere very numerous, and unless in the villi, present no regular sort of arrangement. Thus aberrations from the normal type could not easily be detected, and, moreover, there is nothing in the minute structure to distinguish the original capillaries from those more newly formed.

Hæmorrhages are occasionally found, and more frequently hæmatoidin granules. The former are never considerable and occur in cases presenting well marked hyaline changes. These are the cases, besides, in which new-formation of vessels would be most likely to occur, and in all probability a rupture of one of these accounts in many instances for the hæmorrhage.

Hyaline Degeneration of Veins and Capillaries.—This hyaline change may also attack the veins. Their fibrous tissue walls become swollen up and eventually replaced by a layer of hyaline material. This is frequently associated with a well-marked hyaline degeneration of the connective tissue fibres in the neighbourhood of the vein. The thickening is never very extensive, but the spaces so frequently seen in their walls become obliterated. More serious are the results of this condition when the venules and capillaries are affected. Oeller[39] describes a preliminary proliferation of the endothelial cells subsequent to which the hyaline thickening occurs. Whether such is really the case I cannot say, but there is no doubt that an increase of the endothelial cells is frequently found along with the hyaline thickening; and these two conditions very often lead to obliteration of the venules and capillaries. Probably in some cases, though by no means in the majority, this obliteration is actually brought about by thrombi forming in the altered vessel, these thrombi after a time likewise assuming a hyaline appearance. Later on the hyaline cords may lose their homogeneous character and become distinctly fibrillated. Dilatation of hyaline capillaries is said by W. F. Robertson to occur very rarely, and such I have seen on only a very few occasions.

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[*These illustrations have been kindly lent by the editors of the Journal of Mental Science.*]

EXPLANATION OF PHOTO-MICROGRAPHS.

FIG. 1.

Central part of glomus. (× 26). From a case of puerperal insanity. In the centre is shown the normal arrangement of large and distinct spaces, analogous to the "subarachnoid spaces," or "arachnoid cisterns." Numerous blood-vessels and concentric bodies are also present.

FIG. 2.

Glomus. (× 26). From a case of alcoholic insanity. Here is seen the normal proportion of blood-vessels. The walls of the arteries are thickened from hyaline degeneration. Observe how the fibrous tissue of the walls of the veins very quickly merges into the surrounding spongy tissue, in some cases the trabecular spaces coming quite close to the intima.

FIG. 3.

Irregular forms of hyaline concentric bodies, produced by the coalescence of several spheres. (× 120). From a case of puerperal insanity.

FIG. 4.

Development of a hyaline concentric body from a venule. (× 240). From a case of general paralysis. In centre of photo is seen a venule, the wall of which is enormously thickened from hyaline degeneration. The hyaline circle shows concentric markings, and the interior is packed with proliferated endothelial cells, likewise in a condition of hyaline degeneration.

FIG. 5.

Portion of a cyst of the choroid plexus. (× 140). From a case of general paralysis. To the left are seen the greatly dilated spaces of the pia-arachnoid, lined by degenerated and degenerating endothelial cells. A few degenerated cells are floating in the fluid distending these spaces, and some of the connective tissue trabeculæ show the hyaline change. To the right of this open network, and gradually blending with it, is a dense tissue in which there has been very extensive proliferation of the endothelial cells lining the trabeculæ.

FIG. 6.

Transverse section of a hyaline arteriole. (× 240). From a case of senile insanity. The intima is greatly thickened, and amidst the fibrous tissue may be seen several layers of wavy elastic laminæ.

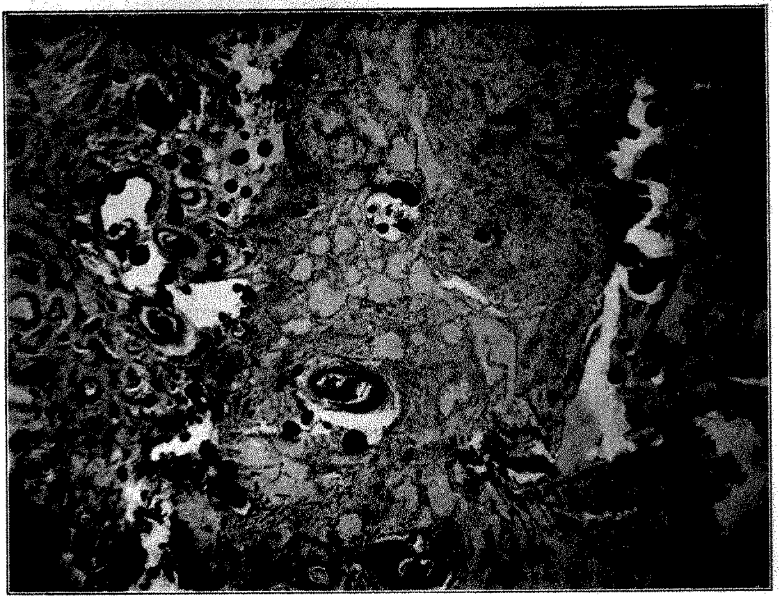

FIG. 1.
Central part of glomus, showing large and distinct spaces. Puerperal Insanity. (× 26.)

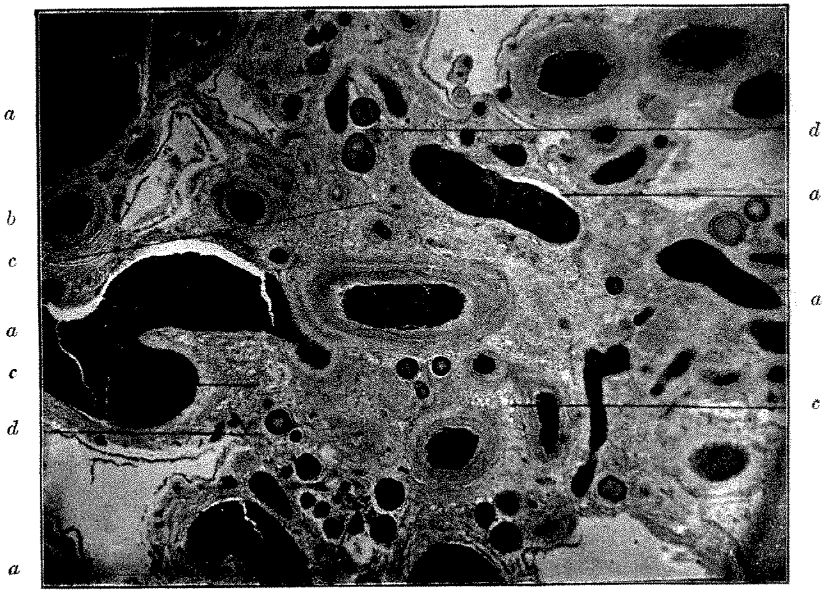

FIG. 2
Glomus showing usual distribution of veins. Alcoholic Insanity. (× 26.)
a, Veins; *b*, Arteries; *c*, Open trabecular arrangement; *d*, Hyaline concentric bodies.

To illustrate Dr. FINDLAY's Paper.

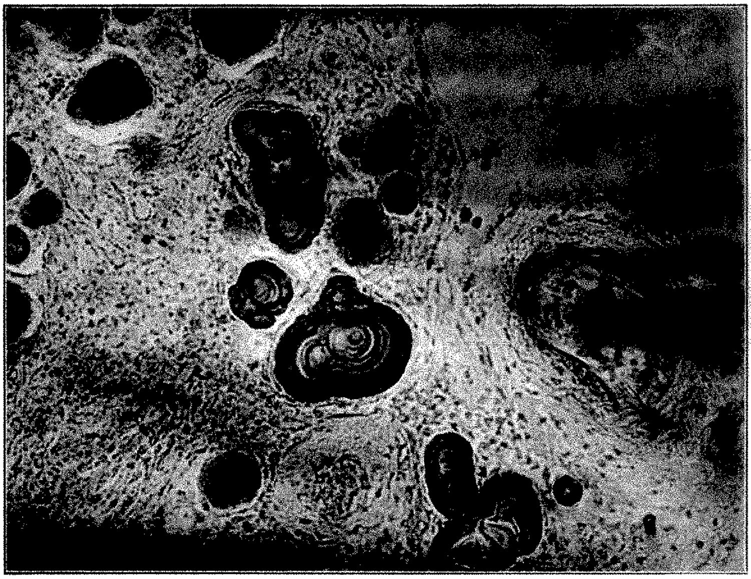

FIG. 3.
Irregular forms of hyaline concentric bodies. Puerperal Insanity. (× 120.)

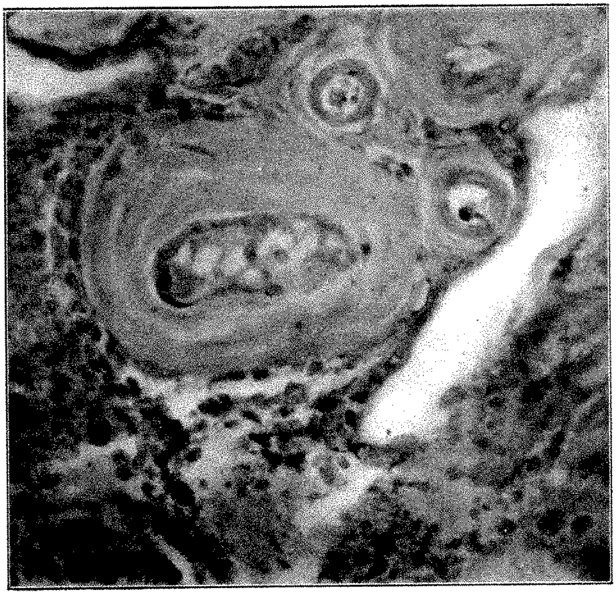

FIG. 4.
Development of hyaline concentric bodies. Wall of venule enormously thickened from hyaline degeneration, proliferation of the endothelial cells. General Paralysis. (× 240.)

To illustrate Dr. FINDLAY'S Paper.

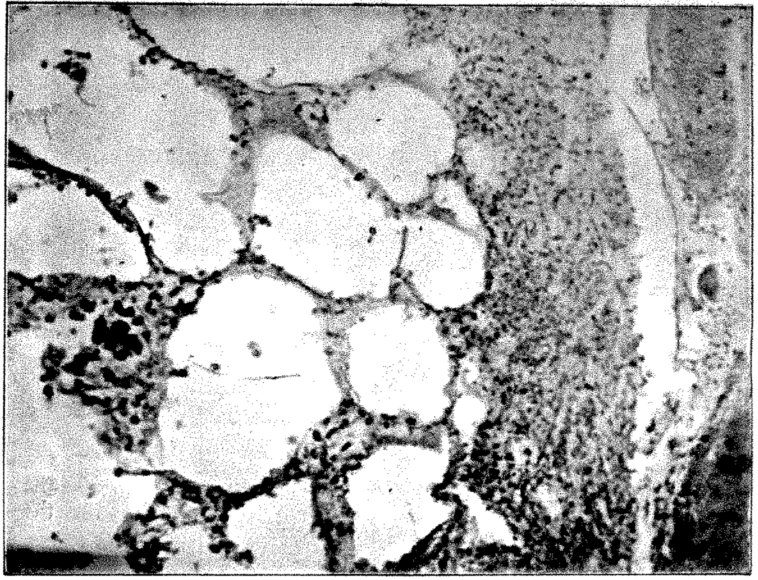

FIG. 5.
Cyst of choroid plexus.

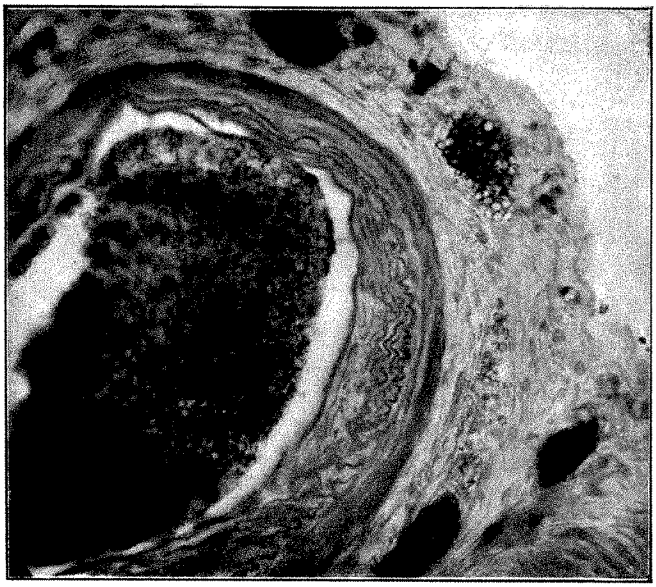

FIG. 6.
Section of arteriole, showing several layers of elastic laminæ.
To illustrate Dr. FINDLAY's Paper.

Critical Digest.

NORMAL AND PATHOLOGICAL HISTOLOGY OF THE NERVE-CELL.

BY W. FORD ROBERTSON, M.D.,

Pathologist to the Scottish Asylums.

INTRODUCTORY note. Recent advances in histological *technique* (p. 204).

I. *Normal structure of the nerve-cell.*

(1) Terminology (p. 207).
(2) Nissl-bodies, or chromophile elements of the cytoplasm (p. 210).
(3) Achromatic or achromophile part of the cytoplasm (p. 219).
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IV. *Addendum upon physiological and pathological deductions.*

THE purpose of this digest is to present a systematic account of the more important observations that have been made during the last five years upon the normal structure of the nerve-cell and upon the morbid changes to which it is subject. Our knowledge of the normal histology and physiology of the neuron as it stood in 1893 was summarised by Professor Schäfer (471) in his presidential address to the Neurological Society delivered in that year and afterwards printed in this journal. In the same year, Aldren Turner (490) and Tanzi (499) published critical digests which dealt with the facts and inductions derived from the study of the nervous system with the aid of Golgi's method. These papers related mainly to the external form of the normal nerve-cell, the course of its ramifications, and its anatomical and physiological relations to other nerve-cells. Since that time, the advances that have been made in our knowledge respecting these points are by no means great. On the other hand, the essentially different subject to which I limit the present digest—the internal structure of the nerve-cell and its alterations in morbid conditions—is one in regard to which there has been an activity of research and a rapidity of progress, probably unparalleled in the whole history of neurological science. As yet the great mass of the observations that have been made are recorded only in papers in the various medical journals, and it will therefore probably be generally conceded that there is need at the present time for some such systematic epitome of them as it is here endeavoured to give. It should be stated, however, that the work that has been done has twice been the subject of critical review on the Continent, viz., by Lugaro (242) in 1896 and by Marinesco (314) in 1897.

In so far as has been practicable, I have studied the original paper to which reference is made. When this has been inaccessible to me—and it has rarely been so except in the case of some papers of secondary importance—I have contented myself with the perusal of the abstracts in such journals as the *Rivista di Patologia Nervosa e Mentale*, *Neurologisches Centralblatt* and *Revue Neurologique*. Owing to the very large number of papers requiring notice, it has been impossible to give the title of all of them in the bibliography, but it is trusted that the reference in the text will in every instance be sufficient to indicate the subject. I have endeavoured to supply a complete review of the work recorded from 1894 to 1898, but I can scarcely hope that I have not omitted to notice some observations of importance. A practically complete classified list of the neurological papers published since 1895 will be found in the very useful *Bibliographischer Semesterbericht*, which is now being issued by Dr. G. Buschan (Fischer, Jena).

In the succeeding pages it will be necessary from time to time to make mention of the histological *technique* employed by the various observers. It will, therefore, probably conduce to clearness if at the outset I give a brief general account of this subject in its relation to the study of the nerve-cell. Most of the methods now in use will be found described in detail in the recent text-books upon histological *technique*, such as those of Bolles Lee and Pollack. With regard to the fixation of nervous tissues in which it is intended to study the nerve-cells, the great weight of authoritative opinion is at present undoubtedly in favour of the use of corrosive sublimate after Heidenhain's method (G. Mann (331), Lugaro, Giuseppe Levi, Lenhossék, Dotto e Pusateri). There are still many, however, who continue to use 96 per cent. alcohol, as originally advocated by Nissl. Another fixing agent that has lately come to be very largely used in the neurological laboratory is formaldehyde, which is sold as a 40 per cent. solution in water under the name of formalin. The original methylene blue staining method of

Nissl (358-362), to the introduction of which is largely due the impetus that has been given to the study of the nerve-cell, has been extensively used by many observers. It has, however, been essentially modified in the hands of some of the best authorities on nerve-cell histology, although still commonly referred to by them as "Nissl's method." Nissl proscribed paraffin embedding. Such high authorities as Lugaro, van Gehuchten, Marinesco and Giuseppe Levi, as well as numerous others, have, however, constantly employed it in their work. Those who have in this respect departed from the *technique* advocated by Nissl have also as a rule substituted another stain for the methylene blue patent B, those most in favour being toluidin blue and thionine. Numerous other staining methods have been employed, chiefly for the demonstration of some particular histological point. Thus, Rosin (446) and Giuseppe Levi have used the Ehrlich-Biondi reagent for the determination of the acidophile and basophile properties of the different constituents of the nerve-cell. Lugaro has specially advocated the use of Delafield's hæmatoxylin and of Heidenhain's iron-hæmatoxylin method for the demonstration of the primitive fibrils of the nerve-cell protoplasm. Elective staining methods for these fibrils have been described by Becker, Held and Bethe. Ehrlich's *intravitam* methylene blue method, which is of much earlier origin than Nissl's method, has also been very extensively used during the period under review, and has been variously modified by numerous workers, among whom may specially be mentioned Dogiel, Semi Meyer, Bethe and Donaggio. Lastly, the chrome-silver and sublimate methods of Golgi have been largely used, not only for the study of the normal cell, but also for the investigation of its pathological changes. Innumerable modifications have been described, some of them undoubtedly of considerable importance. Foremost among these is, beyond question, Cox's modification of the sublimate method, which, according to Lugaro and many other authorities, is the most trustworthy method of this class for the study of pathological changes. Improved processes of blackening the mercurial deposit have added largely to the value of the sublimate methods. Cox recommended the use of sodium carbonate for this purpose, G. Mirto (340) has specially advocated lithium carbonate, and Donaggio (101) sodium or potassium hydrate. The last-mentioned method was afterwards independently described by Bevan Lewis (273).

I. NORMAL STRUCTURE OF THE NERVE-CELL.

(1) *Terminology.*

The term *neuron* is now in general use to denote the whole nerve-cell, including its processes. The suggestion of Schäfer (471) that it should be employed for the axis-cylinder process has not been adopted. Kölliker (229) has objected to Waldeyer's use of the word *neuron* upon etymological grounds and has advocated instead the terms *nervenbäumchen*, *neurodendron* or *neurodendridion*, which, however, have been very little employed by others. Schäfer proposed that the term *nerve-cell* should be used in the same wide sense as *neuron*, and in the writings of most authorities this signification is now generally given to it.

Taking the motor cell of the anterior horn of the spinal cord as the type, we may enumerate the various constituent parts of the nerve-cell as follows:—The nucleus and nucleolus; the Nissl-bodies; the achromatic substance, composing the greater portion of the cell-body, the protoplasmic processes and their gemmulæ and also the axis-cylinder process, its collaterals and terminal arborisations; the pigment; and lastly, the pericellular and endocellular networks of Golgi, granting that they exist as distinct elements. For some of these constituents of the nerve-cell a large number of different terms have been employed by recent writers. The Nissl-bodies have been referred to by Nissl (363) himself as the *visible, formed,* or *stainable part of the protoplasm, the chromatic substance* (Marinesco, Lugaro and others), *the chromophile part of the cytoplasm* (Levi and others), *the chromatophile elements* (Lugaro, Marinesco, van Gehuchten and others), *the chromophilic particles* (Berkley), *the basophile constituent* (Eve), *the* *tigroid substance* (Lenhossék), *the collagenous substance* (van Gieson), &c. The employment of the term *chromatic*, which has been very general, has led many into the belief that the Nissl-bodies are regarded as composed of chromatin. Some writers have indeed maintained this view, but its erroneousness has been fully proved. *Chromophile (part, substance, or elements)* is the term that is probably least open to objection, and it is one that has recently been largely used. It has, however, been employed by Nissl in a different sense, namely, to denote that condition of the nerve-cell which is characterised by abnormally deep staining with his method (a condition which is now generally regarded as due to the action of the fixing agent), and by Flesch to designate nerve-cells that have a very strong affinity for basic dyes (such as the small, dark cells of the spinal ganglia), in contradistinction to those that have not this character, which he termed *chromophobe* cells. These early uses of the word have now, however, been practically abandoned. *Basophile constituent* must be rejected, because, as Nissl and Levi have shown, this substance has only relative basophile properties. Nissl (363) has objected to the terms *granules* and *granular substance* as being in a large measure false.

There is, unfortunately, considerable confusion regarding the terminology of that portion of the nerve-cell which is not coloured by Nissl's staining process, arising chiefly from the difference of opinion that has existed as to its essential structure. The term *achromatic substance* is that which has undoubtedly been most largely employed. Many writers now use the expression *fundamental substance* synonymously with it. Nissl (363) used the terms *invisible, not formed* and *unstainable* substance upon grounds that are now known to be erroneous. In 1896 Marinesco (305) applied the term *trophoplasm* to the achromatic part of the nerve-cell, believing that this part presides over the nutrition of the neuron. The chromatic part he called *kinetoplasm.* Lugaro (242) has pointed out certain objections to these terms. Marinesco in a later paper (322) gives a fuller exposition of his use of them. Recognising with many other authorities that the achromatic part of the protoplasm is composed of two different elements, he divides it into—(1) *the fundamental achromatic substance* and (2) *the organised fibrillar achromatic substance.* He therefore, it will be seen, limits the meaning of the term *fundamental substance.* He now restricts the term *trophoplasm* to this non-organised portion and calls the fibrillar substance the *spongioplasm.* This terminology proposed by Marinesco certainly deserves the most careful consideration. Its general adoption, if justified by histological and physiological facts, would undoubtedly be very useful. It is to be noted that Gowers (182) has recently employed the terms *kinetoplasm* and *spongioplasm* in quite a different way from the distinguished neurologist of Bucharest.

The protoplasmic processes are also referred to as the *dendrites* (His), *dendrons* (Schäfer) and *dendritic processes.* The gemmulæ of the protoplasmic processes have been variously referred to as the *spines, thorns, spinous processes, lateral buds, pyriform processes,* &c. Synonymously with *axis-cylinder process* the terms *nervous process* (Waldeyer), *nervous prolongation* (Lugaro and others) *neurite, neuraxon,* and *axon* (Foster (146) and others) have frequently been employed. Kölliker (229) made certain distinctions in the use of these terms which have not been generally observed by others. He restricted the terms *nerve-fibre process, neuraxon* and *axon* to those processes that become axis-cylinders of medullated fibres, and the terms *nervous process* and *neuropodion* to those that run a short course and do not become true nerve-fibres. The term *neuroplasm* was given by Kölliker to the homogeneous interfibrillar substance of the axis-cylinder of nerve-fibres. It has been applied by Benda (51), Nissl (366) and Bühler (41) to certain elements that they distinguish in the cell-body, which, however, are not strictly identical (see Section I. (2)).

The term *neuropilema* or *neuropil* was applied by His to the dense trellis-work of fine fibrils (mostly collaterals) which occurs in the nerve-centres. Its use has lately been revived in the discussion of the special views of Apathy regarding the constitution of the nervous system.

Foster (146) has proposed that the cell-body should be called the *perikaryon*, and that the connection of one nerve-cell with another by means of a terminal arborisation applied to the cell-body or to the dendrites should be termed a *synapsis*.

(2) *Nissl-Bodies or Chromophile Elements.*

The progress that had been made in the study of the internal structure of the nerve-cell prior to the period under review, as well as up to the earlier part of this period, will be found recorded in such works as those of Lenhossék (277), Dejerine (122), van Gehuchten (168) and Kölliker (229) and also in a paper published by Nissl (364) in 1895. It was only with the introduction of Nissl's methylene blue method (358) in 1892 that the accurate study of the normal chromophile elements of the protoplasm may be said to have begun, and the paper about to be noticed was practically the first record of the results of such study, although Nissl had previously published two papers in which morbid appearances revealed by this method were described (Nos. 358 and 359).

In 1893 Nissl (360), selecting the cells of the spinal ganglia of man for special study, described them as presenting when stained by his methylene blue method a non-coloured fundamental substance, and coloured particles arranged concentrically around the nucleus and having filiform prolongations. These particles were of various sizes, round, oval, angular or irregular in shape. He maintained that the different degrees of affinity for basic stains presented by the nerve-cells, which had led Flesch to divide them into chromophile and chromophobe cells, were to be attributed to the opposite functional states of activity and repose, and not to the fact that they have a different chemical constitution and different functions as Flesch (151) had maintained. In the same year Rosin (446) recorded some observations upon the structure of nerve-cells made with the aid of Biondi's triple stain. He maintained that the body of the cell is composed of two substances which have different staining reactions, dependent, however, not upon morphological but chemical differences. One of these substances he regarded as analagous to basophile granules in the sense of Ehrlich. K. Schaffer (463) pointed out that the cone of origin of the axis-cylinder process differs from those of the protoplasmic processes in being devoid of chromatic substance, an observation which it is now recognised had previously been made by Simarro.

In 1894 Nissl (361) adversely criticised Rosin's work. In another paper (363) he maintained that the so-called granules essentially represented the morphology of the cell, in opposition to the contention of Rosin that they were merely chemical formations resulting from the union of a basic dye with an acid substance in the protoplasm. He denied that they had basophile properties in the sense of Ehrlich, finding that they could be stained with acid as well as with basic dyes. He also gave a further description of the morphological characters of these bodies. Though they presented themselves in many forms and varied considerably in size, they preserved a fixed arrangement. They appeared as irregular particles, smooth or dentate fibres, spindles, wedges, stellate masses, &c. They were grouped together or placed in rows. In some cells they were united into a network. In fusiform cells they frequently formed blocks, which were applied one to either pole of the nucleus (nuclear caps). At the point of bifurcation of the large protoplasmic processes there was generally a triangular mass of chromatic substance (cone of bifurcation). In the same year G. Mann (330) gave a description of the structure of the nerve-cells of the cervical sympathetic ganglia of the rabbit. He described their Nissl-bodies as occurring in the form of numerous short, rod-shaped chromatin granules. He also stated that he had been able to demonstrate by his methyl blue and eosine method bodies which showed characteristic staining reactions, and which had not previously been described. They consisted of dumb-bell shaped elements placed side by side. There were from four to ten of these "bigeminal bodies" in each cell.

In 1895 Nissl (365) pointed out that the nerve-cells may be divided into two great groups in accordance with certain morphological features. Those of the first group, which he called the somatochrome cells, have a distinct cell-body containing colourable particles. Those of the second group, which he termed karyochrome cells, have only a small cell-body containing no colourable particles. He further divided this group into the karyochrome cells proper and the cytochrome cells or granules. He described the various arrangements of the colourable substance in the somatochrome cells and based upon them a classification of these cells (see L (10)). Nissl (364) in another paper, in which he reviewed the position of nerve-cell anatomy and pathology, maintained that the relation of the amount of the substance stainable with basic dyes to the amount of unstainable substance varies in cells of the same kind. This variability of the staining affinity of the cell he again attributed, in the case of certain kinds of cell at least, to differences in functional state. He believed, however, that the condition of chromophilia, or very deep diffuse staining of the nerve-cells, was artificially produced by the fixing reagent. In the same year Lugaro (238) gave a description of the chromatic substance of the nerve-cells of the cervical ganglia of the rabbit as seen in Nissl preparations. He maintained that it does not exist in the form of isolated particles, but is united into a sort of reticulum, or into a figure comparable to the lacunar cavities of a sponge, and that it is not homogeneous, but composed of various elements more or less intensely colourable. Lenhossék (277) described the Nissl-bodies in the cells of the anterior horn of the spinal cord as compact, large chromophile particles and granules distributed throughout the cell-body, and giving to it a peculiar tigroid aspect. He observed differences in the size and number of the particles in different animals. He maintained that the Nissl-bodies are not artificial products, and that they are not granules in the sense of Altmann. In the cells of the spinal ganglia of the ox he found these bodies to occur as very small granules. He could not find the arrangement of concentric layers described by Nissl in the cells of the human spinal ganglion, but only an indefinite differentiation of the particles into an external and an internal layer, the latter being the denser; nor could he confirm the statement that the particles give off fine threads. Held (201) maintained that the Nissl-bodies are composed of three different elements, namely, minute granules, a homogeneous substance and vacuoles. He regarded all of them, however, as artificial products resulting from precipitation determined by the fixing fluid; they did not exist in the form of large masses in the living cell. He based this contention chiefly on the facts that they are not visible in the fresh state, only commencing to form on the addition of water or of fixing agents, and that their morphological characters vary with the fixative employed. He studied the chemical reactions of the Nissl-bodies, making the observation among many others that they are insoluble in mineral acids, acetic acid, warm alcohol, ether or chloroform, soluble in certain other reagents, such as ferrocyanide of potassium and caustic potash. He included them in the group of nucleo-albumins. Becker (38) described in the Nissl-bodies numerous granules, which he demonstrated by the vital injection of neutral red. He likened them to Ehrlich-Altmann granules, and believed that they play an active *rôle* in cellular metabolism. Benda (51) maintained that the structures in the body of the ganglion cells which stain with basic aniline dyes are neither Ehrlich's granules nor specially formed cell-substance, but the undifferentiated protoplasm, the neuroplasm, which is filled in different degrees with basophile granules, and that the neuroplasm is sharply separable from a differentiated fibrillar substance. Dogiel (117) studied the chromophile substance of the nerve-cells in preparations made by his modification of Ehrlich's methylene blue method. He found that it assumes different aspects according to the duration of the action of the stain upon the fresh tissue. At first it appears as fine particles, but later as little masses which give the cell a speckled character.

In 1896 Lugaro (239) contended that the chromatic part of the protoplasm represents an interfibrillar mass, and that the achromatic part is constituted by the thread-mass of Flemming. Thus Nissl's method gives only, as it were, the negative of the true structural configuration of the nerve-cell. Early in the same year Nissl (366) published a paper containing a minute analysis and criticism of the views advanced by Benda. Ramon y Cajal (426) stated that, studying the distribution of the chromatic part of the cytoplasm, both in the phylogenetic series and in ontogenetic development, he was able to observe in it a differentiation, the principal phases of which are as follows:—(*a*) Granular chromatin diffusely distributed without formation of very apparent aggregations; (*b*) Formation of peripheral aggregations placed around a large perinuclear space; (*c*) Formation of perinuclear aggregations; (*d*) Extension of the chromatic aggregations throughout all the cell-body and moulding of fusiform figures parallel to the expansions. Marinesco (305) described the occasional occurrence of fusiform enlargements containing abundant chromatic filaments in the protoplasmic processes of the motor cells of the spinal cord. Lugaro's important review of the position of nerve-cell pathology (242) in 1896, already alluded to, contains some remarks upon Held's views, which deserve quotation here. Lugaro thinks that Held's hypothesis that the figures obtained with the method of Nissl are artificial products due to a precipitation determined by the fixing agent, even if correct, does not in the least diminish the value of the pathological changes observed in the nerve-cell. Every microscopic figure is an artificial product, an image symbolic of certain morphological conditions; if this product is constant, and presents itself in healthy and pathological tissues in a different form constant for each, the different reaction has the value of an exact indication of the pathological alteration. With Held's assertion that the morphological picture varies with the fixative employed he cannot agree, finding that those fixatives, the superiority of which is now recognised, such as 96 per cent. alcohol, formalin and sublimate, give along with the method of Nissl the same structural figures. In the same year Lugaro (244) gave a minute description of the arrangement of the chromatic substance in the different types of nerve-cell in the posterior root-ganglion of the dog (see I. (13)). Juliusburger (220) maintained views regarding the composition of the Nissl-bodies

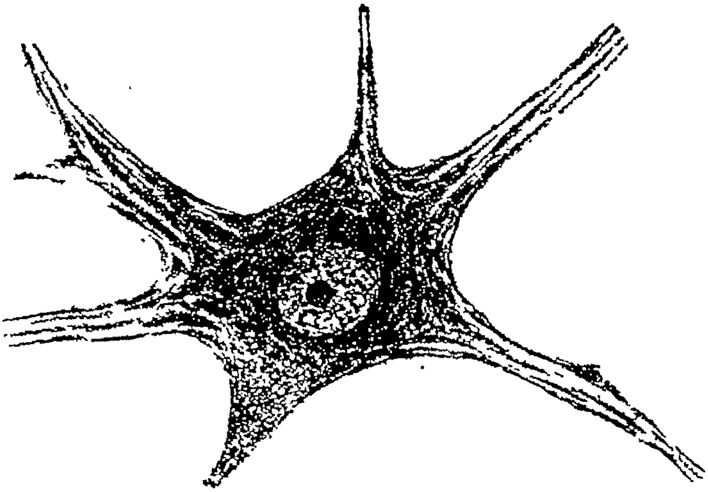

FIG. 1.

Cell of anterior horn of spinal cord of normal rabbit. Sublimate. Thionin. (Lugaro 250.)

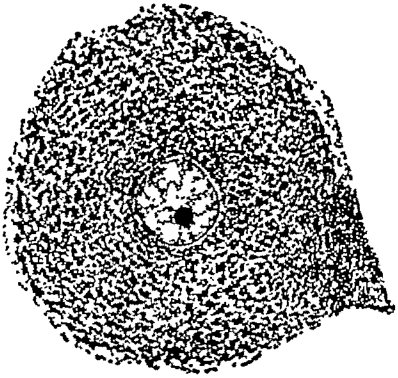

FIG. 2

Cell of spinal ganglion of normal dog. Lugaro's first type. Sublimate. Thionin. (Lugaro 244.)

practically identical with those of Benda. Eve (136) recorded observations upon the arrangement, development and chemical reactions of the "basophile particles," more especially in the cervical sympathetic ganglia of the rabbit. He found that these particles are insoluble in weak sodium chloride solution, but soluble in very weak solutions of caustic soda and acetic acid.

In 1897 Ramon y Cajal (431) gave a minute description of the chromatic elements of the cells of the spinal cord. He stated that the orientation of the chromatic corpuscles is more or less parallel to the outline of the motor-cell, while in the commissural cell it corresponds to the direction of the protoplasmic prolongations. The corpuscles are studded with little projections which penetrate between the trabeculæ of the achromatic substance; they are not homogeneous, but present numerous vacuoles in their interior. There probably exist in them also granules which have the staining reactions of chromatin. From four to six prolongations extend from each chromatophile body, by means of which it places itself in relation with other chromatophile bodies and with the cellular membrane. In the large and medium cells there are two kinds of chromatic elements. One is large, of polygonal form, and sends out prolongations; the other is small, rounded or irregular in form, and is placed at a nodal point of the reticulum of the spongioplasm. Early in this year (1897) there was published the second edition of van Gehuchten's *Le Système Nerveux de l'Homme* (168), in which there will be found a very full and clear description of the chromatic substance of the nerve-cell protoplasm in accordance with the observations made up to that time. In this year, also, Giuseppe Levi (262-263) published an account of his observations upon the comparative histology of nerve-cells. These researches, which extended throughout every class of vertebrate animal excepting birds, have resulted in what is beyond question one of the most important contributions that has yet been made to our knowledge of nerve-cell anatomy. It is impossible in a digest like this to give an adequate idea of the wealth of valuable details regarding the special structural features of the nerve-cells in different animals that this observer has described, and in this sub-section I can only indicate a few of his conclusions regarding "the chromophile part of the cytoplasm of the somatochrome cells." He draws attention to its strong affinity for thionin, a dye which has not distinctly basic characters like methyl-green. He finds that with Biondi's method it is stained, though not intensely, with the acid colour and not with the basic. Therefore it has only weak basophile properties. He finds that the forms assumed by this substance in different animals are very various. It may appear as powdery granules, as more or less large granules, as threads, but more often as masses (*zolle*). Its fine structure in preparations fixed in sublimate is always granular. In different cells of the same animal the chromophile substance preserves a certain uniformity of type. For example, in the guinea-pig the cells of the anterior horn and those of the spinal ganglia have both large isolated chromophile particles; in the dog and ox they contain small diffuse granules; in the dormouse dense spindles. He believes that he has been able to establish the fact that the chromophile substance is deposited in particles, which are the more minute the more voluminous is the cell, independently of the position the animal occupies in the zoological scale. Thus, in the large cells of the ox and in the giant-cells of petromyzon the chromophile substance is powdery, while in the guinea-pig, bat and dormouse its granules are aggregated into large and more or less dense masses. While, as a rule, the chromophile particles are traversed in every direction by the fibrils of the achromatic substance, in certain cases (petromyzon) these two constituents are completely separated from each other. R. A. Fleming (145) has given a good *résumé* of the various views advanced up to this date regarding the nature of the chromatic substance. He mentions that Halliburton and Siegfried (like Held) consider that it is a nucleo-albumin. In the *Rapport* upon the pathology of the nerve-cell which he presented to the International Congress of Medicine held at Moscow, Marinesco (314) gave a precise description of the chromatophile elements of the protoplasm and of their relation to the achromatic fibrillar portion. He stated that these elements, as seen in the large cells of the spinal cord, are disposed concentrically around the nucleus and prefer a polygonal form. The further they are placed from the centre the more elongated do they become, and in the protoplasmic prolongations take a fusiform aspect, their long axis being parallel to that of the prolongations. They are absent from the axis-cylinder process. They give to the cells of the anterior horn a spotted appearance like that of the skin of the tiger. Examined with very high powers, these chromatophile elements appear composed of elementary granules agglutinated by a pale achromatic substance. Van Gehucten (169), in a paper which was likewise brought before the International Congress of Medicine held at Moscow, gives a very minute description of the chromatic substance of the cells of the cord and posterior root ganglia. He regards its elements as forming in the motor-cells of the cord an incrustation upon the nodal points and trabeculæ of the achromatic network. The greater this incrustation becomes the smaller must be the spaces of the network. If it involves several neighbouring trabeculæ and nodal points, there is produced the structure of a chromatic block. Such a chromatic block does not present any regular contour, because fine incrusted trabeculæ extend from it on all sides. The chromatic substance in the cells of the spinal ganglia varies greatly in its form in different animals. It incrusts mostly the nodal points of an achromatic network and thus forms larger or smaller chromatophile granules. Held (202) published an account of further observations upon the chemical reactions of the Nissl-bodies, and maintained his previous opinion against the criticisms that had been made upon them. He found that if a fresh cord is fixed in alkaline alcohol the Nissl-bodies cannot be observed in the cells of the anterior horns. If a piece of cord fixed in this way is placed for some time in an acid solution the Nissl-bodies reappear. He maintained that the formation of these bodies depends upon the acid reaction assumed by the grey substance after death. In life the cells have an alkaline reaction and the constituents of the Nissl-bodies are in solution. If a cord is examined immediately after death no Nissl-bodies can be seen, but they appear immediately on the addition of very dilute acetic acid.

In 1898 Marinesco (322) gave a very full description of the disposition of the chromatic elements in the cells of the sympathetic ganglia; and van Gehuchten and Nélis (176) described the arrangement of those in the various types of cell in the spinal ganglia of the rabbit. In this year there also appeared the important work of Bühler (41) upon the structure of the nerve-cells, a chapter of which is dedicated to the subject of the chromatic elements of the protoplasm. According to Levi (267), who has given a very full account of the contents of this paper, Bühler arrays himself with the majority of observers against the views of Held. He thinks that during metabolism in the nerve-cell there is formed an albuminoid which is soluble in normal salt solution and in alkalies, and is coagulated by the agents that usually coagulate albuminoids. It is distinguished, both in the fresh state and when coagulated, by a specific affinity for the basic aniline colours. It appears as spherules which are often united into more or less dense groups. When the functional processes of the cell are disturbed it either does not form or is formed in an abnormal fashion and dissolves. Timofeew (506) has noted that in birds (cells of spinal and sympathetic ganglia) the chromophile substance is specially abundant. Donaggio (105), in his most recent paper upon the reticulum which he demonstrates in the nerve-cells by means of his own modification of Ehrlich's methylene blue method, has suggested an interpretation of certain of the appearances presented which specially concerns the chromatic substance of the protoplasm. He finds that the reticulum (which corresponds to the spongioplasm of Marinesco) is, in the cell-body and initial portion of the large protoplasmic prolongations, invested by granules which stain more deeply than the threads of the reticulum. He thinks that these granules represent the chromatic substance of the protoplasm in its unaltered form and arrangement. Ewing (135) states that he is convinced "that the chromatic bodies are homogeneous in the natural state, that they make their appearance in finely granular form shortly after death." He further maintains "that the chromatic structures in the cerebral, spinal and spinal ganglionic cells are always found in the form of a reticulum with nodal thickenings, which in the stichocromes reach a considerable volume, covering often several adjoining meshes of the network."

(3) *The Achromatic or Achromophile part of the Cytoplasm.*

It has been freely admitted by the other and more recent authorities that the researches of Flemming (139), of which an account was published in 1882, opened the modern epoch of the anatomy of the nerve-cell (Lugaro, 249, Nissl, 364). Flemming, using the iron hæmatoxylin method of Heidenhain and also staining with Delafield's hæmatoxylin, demonstrated the presence of short undulating fibrils in the cytoplasm of the cells of the spinal ganglia of mammals. He stated that they were continued into the colourable particles, and that they probably formed a network. In certain later writings the priority of Flemming in describing the primitive fibrils has been disputed upon erroneous grounds. Levi (262) has recently drawn attention to the matter and given a clear statement of the facts. He says:—"I think it opportune to point out an error into which those authors have fallen who assert that Flemming was not the first to demonstrate the presence of fibrils in the nerve-cells, but that he merely confirmed an old discovery of M. Schultze (*Stricker's Handbüch*, 1871, Bd. I.). As is known, this author believed that the fibrils are continued into the cell and converge in the manner of rays from the dendrites towards the nucleus without forming anastomoses, and are continued in the axis-cylinder, thus only traversing the cell. To what the fibrils seen by M. Schültze correspond I am not able to say with exactitude; it is presumable that a large part of the striæ described by him were formed by the chromophile particles of the dendrites, as Flemming believes; in any case, it is evident that this structure has nothing in common with that recently described in the nerve-cells, and to endeavour to identify it with any one only contributes to the creation of deplorable confusion."

In 1894 G. Mann (330), describing the sympathetic ganglia of the rabbit, stated that "the protoplasm of the cell consists of a ground substance with a great number of fibrils imbedded in it, which run in bundles and may be traced from one process past the nucleus to another process." He referred also to the existence of an interfibrillar ground substance in which the chromatin granules are embedded. In 1895 Held (201) maintained that, except at the origin of the axis-cylinder, the ground substance of the nerve-cell is never fibrillar. A fibrillar structure is simulated by the honeycomb appearance (vacuolation) caused by certain methods of fixation. Becker (38), by means of a method of his own, obtained an elective staining of the substance which remains unstained in preparations by Nissl's method. He stated that this substance is a direct continuation of the primitive fibrils of the axis-cylinder process into the cell-body and protoplasmic processes. Benda (51) also described a differentiated fibrillar substance in the cell-body and processes. Dehler (106) observed in the cells of the sympathetic of the frog elongated granules, which formed a fibrillar network similar to that described by Flemming. But he found transitions between the fibrils and the chromatic substance, and therefore believed that they were not distinct structures. Lenhossék (277) denied that the ground substance of the nerve-cells contains fibrils, attributing to it a spongy structure. Dogiel (117), using his modification of Ehrlich's methylene-blue method, observed in the ganglion cells of the retina large fibrils, which passed from one dendrite to another. Flemming (140) confirmed his previous observations upon the structure of the spinal ganglia and gave a further description of the fibrils of the nerve-cell protoplasm. He noted, also, the presence of a granular, faintly colourable, interfibrillar substance. Towards the close of 1895 Nissl (370), who had previously attributed to the unstained portion of the cytoplasm an unorganised or granular character, stated that he was now convinced after seeing Becker's preparations that it contained fibrils.

In 1896 Lugaro (239) maintained that there is a protoplasmic texture in the achromatic part of the protoplasm and that the chromatic part passively occupies the interstices left by the achromatic texture; the achromatic part is constituted by the thread-mass of Flemming. In support of this view, he pointed out certain features of the disposition of the chromatic substance which suggest that it fills up spaces left by the fibrils. Moreover, in the part which appears homogeneous in preparations by Nissl's method, a fibrillar structure can be demonstrated by other methods. It has a fasciculated appearance in the processes, a reticular in the cell-body. A further argument in support of this view he drew from the existence of unipolar nerve-cells. In these elements there must be an independent and inverse conduction. The only solution of the difficulty as to how this can occur lies in the hypothesis of the existence of a fibrillar structure and of an isolated conductibility in the single fibrils of tracts apparently homogeneous. In a later paper (242) he described further observations upon the fibrils of the achromatic substance, made with the aid of staining with Delafield's hæmatoxylin and with the iron hæmatoxylin method, in the early stages of chromatolysis, when, owing to disappearance of the chromatic substance, the fibrils of the achromatic part are more easily discernible. Ramon y Cajal (426) expressed the opinion that the fundamental substance, not only of the nerve-cells, but also of the axis-cylinder, is formed of trabeculæ of achromatic substance in which the longitudinal trabeculæ are larger than the transverse, and that the fibrillar aspect seen by others is due to the retraction of the cytoplasm, on account of which there is seen only the longitudinal trabeculæ (Levi, 262). Levi (260), in his studies upon the fuchsinophile granules in the nerve-cells of the spinal ganglia, obtained with Galeotti's staining method a demonstration of fibrils exactly coinciding with those described by Flemming. Lenhossék (280) stated that he had found in the dendrites of the cells of the anterior horn of the spinal cord of the frog and in the cells of Purkinje of mammals three to seven striæ, which were continued into the fundamental substance of the chromophile particles and which simulated a fibrillar structure, but which he maintained could not be interpreted as fibrils (Levi, 262). Flemming (141) described the fibrils of the achromatic substance in the cells of the cord of *gadus callarius*. He was able to satisfy himself that they form a reticulum in the cell-body. Sczawinska (486) found in the protoplasm of the nerve-cells of the anterior horn of the cord of the skate a fibrillar network, not only in the cell-body, but also in the protoplasmic and axis-cylinder processes. W. H. Cox (94) described the arrangement of the fibrils in the cells of the posterior root ganglia as observed in preparations by a new method of his own. The appearances suggested the presence of a network, but he seems to have been unable to determine its existence definitely. Dogiel (118) has distinguished two systems of fibrils in the cells of the spinal ganglia of mammals from results obtained with his vital methylene-blue method. One is peripheral and formed by fibrils which converge in the axis-cylinder process. The other is situated in the central part of the cell. Regarding the cell as a sphere, he looks upon the former as a system of parallels and the latter as a system of meridians.

In 1897 van Gehuchten (168) maintained that the achromatic substance consists of an organised and a non-organised part. The former has a reticular structure and represents the true cellular protoplasm. Lugaro (245), in the course of his studies upon the nerve-cells of the dog in poisoning by arsenic and lead, found that a very clear demonstration of the primitive fibrils could be obtained with Delafield's hæmatoxylin in cells which had undergone partial chromatolysis as the result of the action of the first of these poisons. He gives a minute description of the arrangement of the fibrils in the cells of the spinal ganglia, and formulates certain general conclusions regarding the nerve-cell of which the following are of interest here: The achromatic part of the nerve-cell contains the organs of nervous conduction, the fibrils, which in the protoplasmic prolongations run parallel, and in the body form networks which anastomose in various ways and constitute a true reticulum, the configuration of which varies with the various types of cell. The chromatic part is disposed passively in the interstices left by the achromatic part, so that it gives us a rough negative image of the disposition and course of the bundles of fibrils which enter the cell-body from the prolongations. Levi (262) in his comparative researches upon nerve-cells paid special attention to the arrangement of the fibrils of the "fundamental part." He found that the cells of the spinal ganglia of *bufo* and *zamenis*, and the ventral cells of the cord of *scyllium*, are specially suitable for the study of these fibrils. The differences of arrangement presented in different animals he found to be considerable. He believes that the fibrils are not long and independent, but form anastomoses which are difficult to see, because hidden by the fibrils that interweave in every direction. These anastomoses are less numerous in those parts of the cell concerned more with conduction than with the performance of the specific function, and may be absent in parts exclusively conductive. The bundles of the fibrils in the dendrites go to clothe the superficial part of the cell-body, sometimes passing from one dendrite to another, sometimes turning down towards the deep part of the cell, where the fibrils crossing in every direction form a true network with large meshes. He finds that, as a rule, the axis-cylinder arises from the centre of the cell from an achromatic fibrillar cone which is never in relation with the parallel fibrils of the peripheral portion of the cell, and he therefore associates himself with the opinion of Lugaro (247) that the fibrils of the axis-cylinder originate from the reticulum in the deep part of the cytoplasm. The fibrils of the axis-cylinder are always parallel and only slightly undulated. He has been unable to demonstrate fibrils in the protoplasm of the karyochrome cells. He describes the vortices of the nerve-cells of *bufo* and compares his observations with those of Lenhossék upon the occurrence of a centrosome and sphere in the cells of the spinal ganglia of *rana* (Section I. 4). Ramon y Cajal (431) described the arrangement of the achromatic reticulum in the cells of the spinal cord. He drew attention to the occurrence of little chromatophile bodies at the nodal points of the reticulum of the cell-body, excepting at the origin of the prolongations. He could not exclude the possibility that this reticulum is produced by coagulation of the protoplasm by fixatives, but thought there were many considerations strongly in favour of the view that it is preformed. Nissl (371) described the fibrils to be observed more especially in the cells of the anterior horn of the spinal cord of the calf in preparations by Becker's method. He expressly stated that it is possible to follow the continuity of numerous single fibrils through the whole cell-body. No difference could be observed in the appearance of the fibrils in the dendrites and neurites. Marinesco (313) described in the achromatic portion of the nerve-cell a ground substance and a substance which has a fibrillar structure in the processes and a reticular structure in the body of the cell. There is an anatomical continuity between this network and the fibres in the processes. In another paper (316) he stated that the formed achromatic substance (as seen in the cells of the spinal cord and spinal ganglia in peripheral chromatolysis) is constituted by a network which gives the cell a spongy appearance. The fibrils are attached to the periphery of the cell and to the wall of the nucleus. There are nodes at the points of intersection of the threads. The achromatic network (the spongioplasm) is the frame-work of the cellular edifice. Its disposition and texture regulates the form of the chromatophile elements. In the *Rapport* (314), which he presented to the International Congress of Moscow, he gives a detailed description of the achromatic fibrils, specially mentioning the occurrence of little chromatic swellings at the points of intersection of the threads, which he terms "nodal points." He defines the relationship between the fibrils of the nervous prolongation and those of the network of the cytoplasm. The parallel fibres of the axis-cylinder as they enter the cell break up into several bundles, of which one turns towards the centre, the others towards the periphery of the cell. They give off branches by which they establish an anatomical continuity with the network of the cytoplasm. Van Gehuchten (169), in his communication to the Congress of Moscow, described the achromatic network of the nerve-cell as forming not only the essential part of the cell-body, but also the regular constituent part of the processes. In the protoplasmic processes the fibrils have a somewhat granular appearance, while in the axis-cylinder they are regular and distinct. Held (202) believes that the nerve-cell protoplasm and its prolongations have an alveolar or honeycomb structure, and maintains that the appearance of fibrils is artificial. Lenhossék (281) maintained his opinion that the achromatic part of the nerve-cells of the spinal ganglia of mammals has not a fibrillar character, but only a finely honeycomb structure. He admitted, however, the presence of fibrils in the axis-cylinder and in its cone of origin. Flemming (142), in a paper in which he criticised Lenhossék's views, maintained that the fundamental substance of all nerve-cells has a fibrillar structure. The fibrillation is longitudinal and radiated at the point of origin of the processes, reticulated in the rest of the cell-body. Pugnat (393) studied the spinal ganglia of reptiles and confirmed several of the observations previously made by Levi regarding the arrangement of the fibrils. Bethe (46) described in certain invertebrates and in the frog the complete or partial passage of the fibrils through the body of the nerve-cell from process to process without the formation of a network.

In this place the description of the primitive fibrils given by Apathy (8) would in ordinary course require some reference. But it will be more convenient to postpone consideration of the peculiar views advanced by this observer to another section (I. 9).

Writing in 1898, Cox (95) distinguishes in the cells of the spinal ganglia of the rabbit two kinds of fibrils, one long and straight, similar to those of the cone of origin of the axis-cylinder, and running in the achromatic intervals, the other short and tortuous and enclosed in the chromatic particles. He is inclined to believe that the fibrils are independent and that the appearance of a reticulum is a fallacious one (Lugaro, 253). Lenhossék (282) has now been able to obtain a satisfactory demonstration of a fibrillar structure in the nerve-cells of the frog and an indication of it in the peripheral stratum of the cells of the spinal ganglia of mammals. Auerbach (9) describes in the cells of the spinal ganglia of the guinea-pig and rabbit a reticulum of fine fibrils with swellings at the nodal points. He has observed these nodal points in the cone of the axis-cylinder as in the rest of the cell, and believes, therefore, that it also is constituted by a fine reticulum. He states, however, that he is convinced that the structure is not truly reticular but alveolar, and that the appearance of fibrils is due to the action of fixatives. Ramon y Cajal (434) has observed in the cells of the spinal ganglia of the cat, with staining by Delafield's hæmatoxylin, an evident fibrillar structure of the axis-cylinder process continuous with a reticulo-fibrillar structure extending throughout the body of the cell (Lugaro, 253). Arnold (18), from results obtained with a special method of fixation, is persuaded that the achromatic substance has no definite fibrillar structure, although it contains some threads which appear to be continuous with the thread-net of the nucleus. Bühler (41) thinks that two kinds of fibrillar formations are to be distinguished in the nerve-cell protoplasm. Firstly, there are long fibrils continuous with those of the axis-cylinder and constituting the paths of conduction; secondly, there are short fibrils anastomosing in a reticulum which pervades all the cell, including the axis-cylinder, and which constitutes the fundamental substance of the cell, the neuroplasma (Lugaro, 253). Bethe (47-48) describes the pictures obtained by means of his new staining method for the primitive fibrils. The fibrils of the axis-cylinder are quite isolated from each other. The substance between them is homogeneous. In the body of the nerve-cells the fibrils likewise appear as well individualised, deeply-stained structures. In some cells it is possible to follow all the primitive fibrils continuously from process to process through the cell-body. In other cells their course cannot be made out. He rarely saw any evidence of division of the fibrils. There is no network of fibrils, but only a felt-work composed of isolated threads. He could not find any junction of them with each other. A large number of the fibrils of one dendrite pass into a neighbouring dendrite, in some instances without ever really entering the cell-body. He describes the course of the

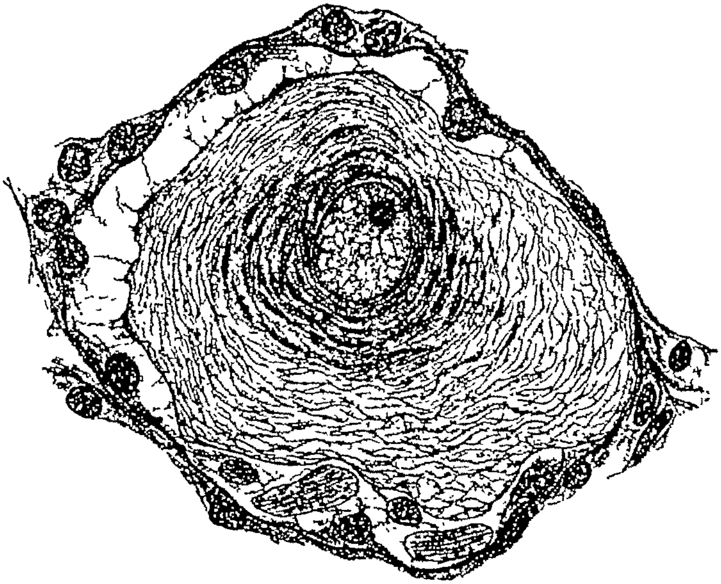

FIG. 3.

Cell of spinal ganglion of dog poisoned with arsenic, showing concentric arrangement of chromatic particles and fibrils. Section in the plane of the course of the fibrils. Owing to peripheral chromatolysis the fibrils are distinctly visible. Sublimate. Delafield's hæmatoxylin. (Lugaro 253.)

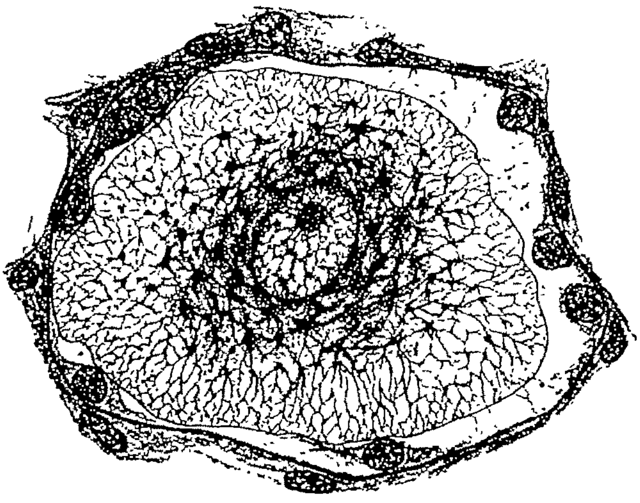

FIG. 4

Same as Fig. 3, except that the section is in a plane perpendicular to those in which the concentric fibrils run. (Lugaro 253.)

fibrils in the various forms of nerve-cell. Lenhossék (284) considers that confirmation of these observations of Bethe is required before they can be accepted as accurate. Marinesco (322), in describing the achromatic reticulum in the sympathetic ganglia, expresses the opinion that the nodal points are formed by true enlargements at the crossing of the fibrils, and therefore should not be thought to be of the same nature as the blocks of chromatic substance. Lugaro (250) directs attention to the beautiful demonstration of a reticulo-fibrillar structure that can be obtained by hæmatoxylin staining of nerve-cells, of which the chromatic part has been altered by experimental pyrexia, and gives a further description of the appearances presented by the primitive fibrils. The same authority (253), in his important paper upon the nerve-cells of the spinal ganglia of the dog, passes in review the previous observations upon the structure of the fundamental substance, and records results of further investigations of his own. He states that there can now be recognised as generally predominant the tendency to admit a reticulo-fibrillar structure, although with regard to certain points there is still considerable disagreement among the individual observers. He himself defends the reticulo-fibrillar theory against that of independent fibrils. He thinks that the various discordant opinions regarding the fibrillar structure are to be attributed largely to erroneous interpretations of the different aspects presented by different cellular types, and even by the same cell from different points of view. The aspect of the fundamental substance varies in different parts of the cell and also according to the direction in which the section of the cell is made. In one plane there may appear a structure of concentric fibrils and in a plane perpendicular to this a reticular structure. This fact has been already noted by Flemming (142). The greatest differences of aspect in the structure of the fundamental substance are, however, those due to difference of cellular type. He gives a minute description of the arrangement in each of the five different types of cell recognised by him in the spinal ganglia of the dog. He incidentally states that the chromatic thickenings at the nodal points do not constitute an integral part of the reticulum, and that they have only a relation to the fibrils of simple super-position. It will be seen that upon this point his opinion differs from that of Marinesco. In all the types the fibrils of the axis-cylinder break up among the fibrils of the cytoplasm, joining with them and thus gradually losing themselves in the reticular formation. He thinks that the different types of penetration of the axis-cylinder described by Cox (95) are but different sectional aspects of the same mode of penetration. He also thinks that the conclusions of Bühler and of Cox regarding the existence of two kinds of fibrils are founded on false interpretations of the different aspects that the same cell can present in different parts and from different points of view. Levi (266), in the course of his study of the changes occurring in the nerve-cells of cold-blooded animals during hibernation, obtained some very clear pictures of the arrangement of the fibrils, which he describes in minute detail. A large part of this paper is taken up with a comparison of the author's observations upon the structure of the vortices with those of Bühler, a subject which will be dealt with in the next subsection. The observations of Donaggio (105) upon the cellular reticulum revealed by a special method will also be more conveniently considered in another subsection (I. 6). Ewing (135) admits the existence of a reticulum in the cell-body, but he regards it as a chromatic reticulum rather than an achromatic. "The strictly achromatic substance of the cell" he describes as granular both in the cell-body and in the axis-cylinder process. Gowers (182) has recently taught that the primitive fibrils pass through the body of the cell without interruption. He bases this contention chiefly upon the observations of Max Schultze.

The gemmulæ of the protoplasmic processes.—As these structures form a part of the achromatic substance of the nerve-cell, they require notice in this place. The recent observations which specially relate to them are not numerous. The most important are undoubtedly those of Hill (204-205) and Lugaro (252). Hill notes the fact that S. Meyer (345) could not find them in preparations by Ehrlich's methylene blue method, and therefore questioned their existence as real structures; and that, on the other hand, Ramon y Cajal (425) observed them by this method both in the young animal and in the adult. The view of Kölliker (229) that they only occur in the adult as artefacts is now quite untenable. Ramon y Cajal (425) made use of a modification of the methylene blue method for their demonstration, and expressly states that the Erlich-Dogiel process does not reveal them, but shows varicosities upon the protoplasmic processes which he regards as a *post-mortem* product due to the action of the air. In a later paper (429) he gives a further description of the gemmulæ as seen in his methylene blue preparations, and states the conclusion that they serve to increase the surface of connection of the protoplasmic arborisation. Hill thinks that the thorns are organic structures which are not shown in their entirety by the chrome silver method, and that the typical form of a rod with a dot at the end is due to a *post-mortem* change in the tissue. He describes the numerous variations in form which they present. He believes that they are really the ends of unstainable nerve filaments surrounded by a film of staining cell-plasm. He has observed that in the cells of Purkinje in the skate they are replaced by long striæ streaming away from the protoplasmic process on either side. Lugaro (252) has demonstrated the functional mobility of the gemmulæ, their general expansion during sleep, and their contraction under the influence of certain stimuli. The results of his observations, and the technique employed, exclude the possibility that their typical appearance is one artificially produced by *post-mortem* change.

(4) *Centrosome and Sphere of Lenhossék.—Vortices of Levi.*

In 1895 Lenhossék (278) described in the cells of the spinal ganglia of the frog a figure to which he applied the term *centrosome and sphere*, and which he demonstrated especially in iron hæmatoxylin preparations. He found that in certain cells the nucleus is eccentric, and that on the side to which the greater part of the protoplasm is placed there is a concentric arrangement of the protoplasm. The central point of this figure, the *centrosome*, is somewhat granular, and surrounding it there is the more homogeneous *sphere*. It is to be borne in mind that at this period Lenhossék denied the existence of fibrils in the body of the nerve-cell. Dehler (106) shortly afterwards confirmed Lenhossék's observation, and similar figures were described by Bühler (40) in *lucertola*, by J. Schaffer (470) in *petromyzon*, and by Lewis (271) and Maclure (354) in the nerve-cells of invertebrates.

In 1897 Levi (262), in the course of his comparative researches, observed in the protoplasm of the cells of the spinal ganglia of the toad the occurrence of a spiral vortex composed of converging fibrils, and having a distant resemblance to the centrosome and sphere described by Lenhossék in the frog. He observed similar figures in the frog and in *zamenis*, but they were less distinct. He states that he is satisfied that what Lenhossék regarded as a homogeneous sphere is really composed of a vortex of fibrils, and that his centrosome is a transverse section of the axis of this vortex. He therefore maintains that one cannot give to this figure the significance either of a centrosome or a sphere, more especially since he has been able to trace the fibrils of the vortex into direct relationship with the origin of the axis-cylinder. This consists badly with the meaning that is commonly given to the term *centrosome*, *i.e.*, a formation which, at least at a certain period of ontogenetic development, takes an active part in the reproduction of the cell. In his paper upon karyokinesis in the nerve-cell, Levi (264) maintained the same view regarding the nature of this so-called centrosome and sphere. He could see no reason for doubting that the centrosome of the somato chrome cells, like that of the *kernzellen* (in the case of which he has proved the point) resides in the nucleolus. Bühler (41) in his work on the nerve-cell, devotes a chapter to the subject of the concentric figure described by Lenhossék, and entirely confirms Levi's statements regarding it. He also gives a description of another structure which he was the first to observe in the nerve-cell (40), namely, the "centrirte system" of Heidenhain. "It is a system of organic rays with central corpuscles and microsomes." It is placed between the nucleus and the inferior pole of the cell, but resides in the proximity of the inferior margin of the nucleus. Often it is double, and always lies on the principal axis of the cell, or in immediate proximity to it. Its presence in the cells of the toad and frog is constant (267). Szczawinska (487) has recognised in the nerve-cells of the skate figures similar to those described by Levi and Bühler. Levi (266), in his recent paper upon the changes in nerve-cells during hibernation, gives a very minute description of the vortices as they occur in the toad, and compares his description with that of Bühler, which differs in certain points of detail, more especially as regards the relations of the "rectilinear fascia" and terminal spiral of the vortex to the axis-cylinder process. He now recognises that it is only during hibernation that a clear view of these formations can be obtained, as at other times they are obscured by the chromophile elements. His description of the fibrils of the vortex and their relation to the axis-cylinder and nucleus is of much interest, but scarcely admits of being epitomised.

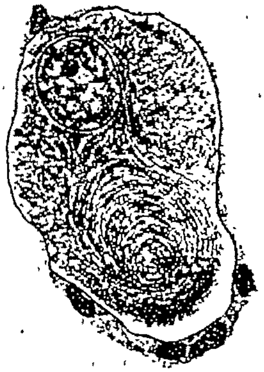

FIG. 5.

Cell of spinal ganglion of *Bufo vulgaris*. Winter. Shows the spiral vortex in oblique section. (Giuseppe Levi 266.)

(5) *Physiological Pigment.*

No very important light has recently been thrown upon the question of the nature of the physiological pigment of the nerve-cell. The only paper that has appeared on the subject during the period under review seems to be that of Pilcz, although there have been numerous incidental references to it. Schäfer (471) maintained that the presence of pigment is not a sign of decadence, but rather one of activity. Pilcz (392) has distinguished two kinds of nerve-cell pigment, which are different as regards their development, and react differently to staining reagents. One is pale yellow, and occurs in the cells of the cerebral cortex, basal ganglia, cord and spinal and sympathetic ganglia. The other is dark brown, and is present in the cells of the locus cœruleus, substantia nigra of Sœmmering and nucleus of the vagus. These two kinds of pigment are not different forms of the same substance, but of an entirely different nature. The yellow pigment is blackened by osmic acid, the brown is not. Neither of them are hæmatogenous. He has studied the period at which these pigments make their appearance in development. The brown pigment first appears in the cells of the locus cœruleus at the twelfth month. In general it appears at an early period of life, and ceases to increase after a few years. On the other hand, the yellow pigment is first seen (in the spinal ganglia) about the sixth year, and continues to increase throughout life. In the lower animals this pigment is much less abundant than in man. It is never found in the cells of Purkinje. Hutchison (209) found that an amount of pigment, far in excess of the ideal standard, was present in nearly 50 per cent. of presumably healthy human brains. Rosin (447) found that the yellow pigment in the nerve-cells of the human cord is blackened by osmic acid, but that this reaction does not occur if the preparations are first treated with ether. He therefore thinks that it is partly of a fatty nature. Colucci (89) states that chemical reactions prove that the yellow globules in nerve-cells are not fat. They may, however, undergo a fatty metamorphosis and then a black reaction is obtained with osmic acid. He regards them as a manifestation of cellular metabolism. It has not been proved that they are true pigment granules such as those in the cells of the locus niger, &c. Marinesco (318) believes that the yellow substance in the nerve-cells arises from a transformation of the chromatophile particles, and that it is allied to fat. He notes that it stains with basic fuchsine, with hæmatoxylin in Weigert's method, and with osmic acid. Lord (289*a*) holds that the pigment of the nerve-cell results from fatty degeneration of the "ovoid bodies" (chromophile elements).

(6) *Golgi's Pericellular Reticulum.*

In April and July of last year Golgi (159-160) made two communications, in which he described two new structural features which he has observed in the nerve-cells in preparations by his rapid silver method, or by special modifications of it. The first consists of a peculiar reticular investment of the cell, the second of an entirely separate reticulum within the cell-body. On account of the great interest of the subject, I think it is well to give a somewhat detailed account of these observations here. I am indebted to Professor Golgi for very kindly sending me reprints of his papers.

The pericellular investment (159) is a very delicate structure formed of a substance clearly differentiated from the cell-body. It sometimes appears as a reticulum, sometimes as a continuous homogeneous stratum, or as closely applied squames. Not rarely it presents striations which might be interpreted as fibres crossing over the cell-body. Most frequently it has a finely reticulated structure, with round, uniform, regular meshes. It forms a cuirass which clothes not only the cellular body but also the protoplasmic prolongations, along which it may be followed even to the subdivisions of the second and third order. Upon these, however, it loses its reticular aspect and becomes a uniform stratum. The cellular substance, including the prolongations, remains colourless and transparent. The investment is seen in its most characteristic form upon the cells of the spinal cord, nuclei of the medulla, dentate nucleus of the cerebellum, &c., but it may be seen upon all varieties of nerve-cell, even the smallest. The cells of Purkinje show it generally as a continuous investment or composed of fine little squames. In the cells of the cerebral convolutions it is commonly uniform and continuous, although the reticular form may also be observed in some. Golgi states that in 1882 he expressed the opinion that it is probable that the nerve-cells possess an investment of the nature of neuro-keratin. In 1893 he spoke more decidedly regarding the existence of such an investment, and invoked it as an argument against the theory of transmission of the nervous current by contiguity (156). In 1895 Lugaro (237) described a similar appearance of the cells of the dentate nucleus of the cerebellum, stating that in silver preparations these cells appear as if invested by a brown shell, which is homogeneous and riddled with holes. Golgi refers also to a somewhat recent paper by Martinotti (299), in which there is described a similar reticular investment of the nerve-cells of the spinal cord which the author thinks may be composed of neuro-keratin. Shortly after Golgi made his first communication, Lugaro (251) published a reply to it on account of certain references which it contained to his observations and views. He points out that he did not give to the structure in question the value of an integral part of the nerve-cell (as Golgi seems to do), but only that of an interstitial substance. More recent observations have still more fully convinced him of the correctness of this view. He finds that the aspect of a cellular investment is only obtained when the cells are at a certain distance from each other. Where they are crowded together the apparent investments tend to become confluent, so that there results that picture which Cajal described, and compared to the aspect of a honeycomb. He cannot affirm with certainty what is the nature of the part that colours, but is inclined to regard it as an interstitial liquid.

The reticular figure described by Donaggio (102-104) has certain points of resemblance to Golgi's pericellular investment, but, as he has lately (105) identified it with the achro-

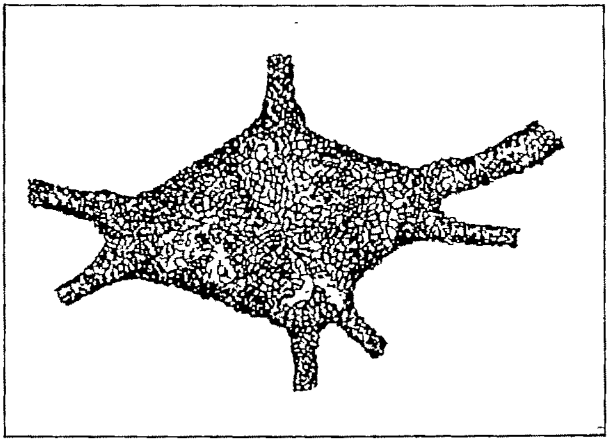

FIG. 6.

Nerve-cell with reticular investment. Cell of anterior horn of spinal cord of cat. (Golgi 159.)

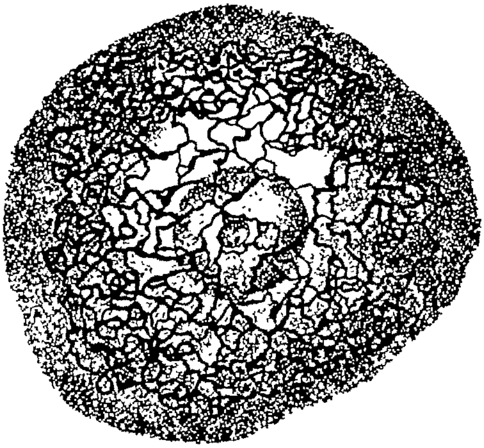

FIG. 7.

Spinal nerve-cell with internal reticular apparatus. From a ganglion of adult dog. (Golgi 160.)

matic reticulum, and as it has to be compared also with Golgi's internal reticulum, I defer consideration of it to the next subsection.

(7) *Golgi's Endocellular Reticulum.*

Golgi (159), in the first of his two recent papers just referred to, describes this structure as a delicate and beautiful reticulum hidden within the cell-body. It has a characteristic aspect on account of which, if the reaction happens to be partial, even little fragments of it can be recognised. It is best examined in mounting media of a lower refractive index than Canada balsam, such as glycerine. It consists of threads of irregular thickness, often somewhat tortuous, which freely anastomose with each other. Between its peripheral limits and the surface of the cell there remains a zone of clear cell-protoplasm. While externally the reticulum is sharply limited, towards its inner aspect, around the nucleus, the threads dip down to different levels. Some of those derived from the peripheral plane present short offshoots which terminate as delicate pyriform swellings. Similar swellings may occur in the course of the threads, more especially at the nodal points. The reticular body has in relation to the whole cell a definite orientation, which, however, presents certain differences in the various categories of cells. In the cells of Purkinje (in which alone up to this time he had made an extensive study of it) the reticulum tends to assume the form of a pear, with the narrow end directed towards the molecular stratum, in correspondence with the point of exit of the large protoplasmic prolongation, in which the various threads run together into one, two or three terminal threads.

In his second paper (160) he states that he believes that this internal reticulum occurs in all the principal categories of nerve-cells and gives a minute description of it as it appears in those of the spinal ganglia of the dog. Its characters here are very similar to those already described in the cells of Purkinje, but, at the same time, they present characteristic differences. It has a globose form, adapting itself (as in other situations) to that of the cell, and it has no special orientation. The reticular constitution is less distinct, giving place to what is rather an irregular filamentous apparatus, complexly convoluted, the threads of which it is difficult to trace. There is undoubtedly, however, the structure of a network. With advancing age, the reticular character seems to become more pronounced. Some of the threads are very fine and of regular thickness, others in the same cell may present a succession of dilatations and constrictions. They may give off some lateral processes which may terminate after a short course in rounded or oval

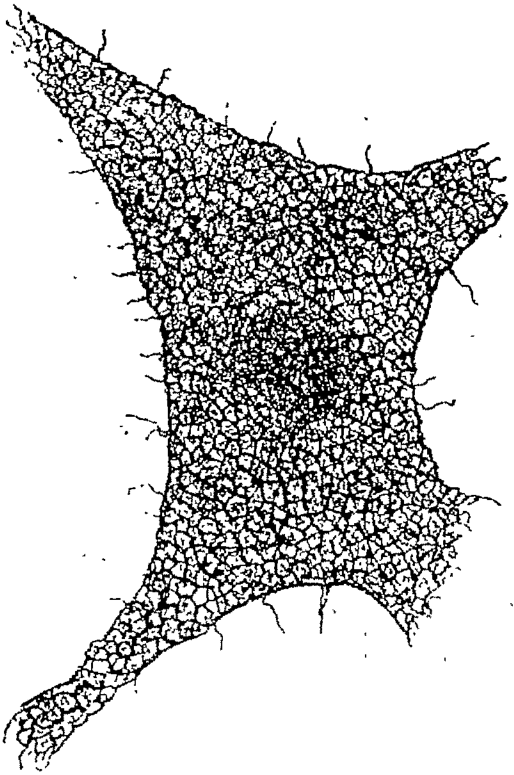

FIG. 8.

Nerve-cell of anterior horn of spinal cord of dog, showing reticulum. The original is in colour. Donaggio's methylene blue method. (Donaggio 105.)

swellings. There is generally a clear zone around the nucleus, but occasional threads appear to terminate in contact with it. He believes that this reticulum is something absolutely different from the Nissl-bodies and primitive fibrils described by others.

Donaggio (102) in 1896, by means of a modification of the vital methylene-blue method, obtained in the nerve-cells of various mammals a demonstration of a fine reticulum, extending throughout the cell-body and protoplasmic prolongations and connected on the one hand with the nuclear network and on the other with fibrils outside the cell. Two years later (104) he described this reticulum more minutely, but came to no very definite conclusion regarding its significance. Quite recently he has published a third paper on the subject (105). He now considers that the reticular figure corresponds to that of the achromatic reticulum of the protoplasm. He has observed, however, that it is most brightly coloured in those parts in which the chromatic substance is known to be most abundant, that is to say, in the cell-body and initial portion of the protoplasmic prolongations, while in the branches of the protoplasmic prolongations it is not visible, and in the cone of the axis-cylinder it is constituted by only very faintly-coloured threads. Further, the deeply-coloured threads present a granular surface, and some cells show an initial formation of chromatic particles. He therefore concludes that the network is formed of threads which consist of two substances, one which is deeply coloured with methylene-blue and corresponds to the chromatic substance shown by Nissl's method, and one which is colourless in preparations by that method. He differs from the opinion of Held, according to which the chromatic substance is dissolved in the protoplasm, and maintains that its normal disposition is on the threads of the achromatic reticulum and that it is for this reason that his method, which does not alter this original disposition, reveals the reticulum. He thinks that up to a certain point a comparison is possible between this reticulum and the two described by Golgi. He cannot, however, by his method see any difference between the external portion and that in the deeper part of the cell. There appears to be only one continuous structure.

Superficial reticular formations analagous to that described by Donaggio have been described by Nissl (374) and Bethe in preparations by the method of the latter. These authorities maintain that these reticula do not belong to the nerve-cell but to the interstitial nervous network which they believe to occur throughout the grey substance (257). Ramon y Cajal (435) opposes this view, and maintains that the pericellular reticulum is merely the more superficial and coarser part of the spongioplasm to which the colouration is sometimes limited in preparations by Erhlich's method. It belongs to the cell and has no connection with the nervous filaments that surround it. He regards the figures described by Golgi as produced by colouration of the interstitial cement, of the superficial network, or, in certain instances, of pericellular nests. In any case, there is no reason to consider the superficial network as either an isolating investment or as a pericellular plexus (257).

(8) *Nucleus and Nucleolus.*

Of the many important contributions that Giuseppe Levi has made to our knowledge of the normal anatomy of the nerve-cell, there is probably none more valuable than the clear and precise description that he has given of the structure of the nucleus. Previous to his taking the matter up, the study of this portion of the nerve-cell had been comparatively neglected, and all descriptions that had been given of it were more or less inaccurate and incomplete. The publication of his first paper on the subject in 1896 may justly be said to mark one of the important epochs in the history of the progress of our knowledge of nerve-cell anatomy.

Flemming (139), in his early paper upon the cells of the spinal ganglia, expressed the belief that both the nuclear membrane and nucleolus are rich in chromatin. Nissl (360) in 1893 described a nuclear membrane, a reticular framework, from one to three nucleoli and also accessory nucleoli. In the same year, Rosin (446), basing his conclusions upon results obtained with Biondi's stain, maintained that the nucleus and nucleolus are neutrophile. In 1894 Nissl (361) differentiated in the nucleolus a delicate external layer, which stained deeply, and a central colourless part. In 1895 Lenhossék (277) described a very delicate nuclear membrane and a faintly-staining nuclear reticulum. In the nucleolus he distinguished a group of from three to five punctiform, strongly colourable endonucleoli. Dehler (106) noted at the periphery of the nucleolus a deeply-staining zone. Roncoroni (443) described in the nuclei of some of the pyramidal cells of the cerebral cortex the occurrence of a sharp line, coloured deep blue in methylene-blue and eosine preparations, and extending sometimes from one pole of the nucleus to the other. He thought that it was probably composed of chromatin. Lugaro (240) maintained that Roncoroni's line is nothing more than a fold of the nuclear membrane, due to shrinking of the nucleus, generally from alcohol hardening, and that staining reactions prove that it is not composed of chromatin. Roncoroni (444) defended his original opinion against the criticisms of Lugaro, who, in turn, replied with further arguments in support of his contentions (241). There can be little doubt that Lugaro's view of this matter is the correct one.

In 1896, Ramon y Cajal (426), from studies with the method of Nissl, concluded that the nucleus of the nerve-cell undergoes, along with its differentiation, a process of simplification consisting in a progressive concentration of all the nuclein in one or two spherical nucleoli, and that it is probable that nerve-cells with the nuclein thus concentrated have lost the power of proliferation. He believed that in the large cells the nuclear contents were devoid of nuclein, but that, on the other hand, the nucleolus was formed entirely of nuclein, which, however, was modified in the central portion by long mitotic repose. Levi (259) published his first paper upon this subject contemporaneously with the preceding. He pointed out that Rosin's conclusion that the nucleus and nucleolus of the nerve-cell are neutrophile is in contradiction to established views regarding the structure of nuclei in general, since it is now believed that the chromatin (or nuclein) of the nucleus has affinities for the basic aniline dyes, the nucleolus for the acid. He considers that Rosin used Biondi's stain in too concentrated solution, and therefore obtained reactions which were largely artificial. It is now known that for elective colouration dilute solutions which stain slowly and progressively are always to be preferred. He has himself employed this progressive method of colouration with Biondi's stain (after sublimate fixation) and has obtained results entirely different from those of Rosin. He finds that in the somatochrome cells all the different elements—including the Nissl-bodies and the achromatic part of the protoplasm, the nuclear membrane and nuclear granules or network—take the acid stain (acid fuchsine and orange G), excepting from two to four particles adherent to the nucleolus, which take the basic stain (methyl green). The large globular nucleolus (or nucleoli, as there are occasionally two), apart from these particles, is very strongly acidophile. The basophile particles vary considerably in form and volume. They may have the aspect of semilunar bands or of spherical masses, or may assume any intermediate form. He has never seen them detached from the nucleolus, nor has he seen other basophile particles among the contents of the nucleus. He describes the special features of the basophile particles in the somatochrome cells of different regions. In the anterior

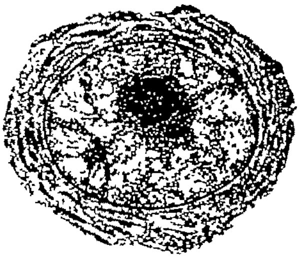

FIG. 9.

Nucleus of nerve-cell of anterior horn of spinal cord of guinea-pig, showing basophile particles attached to the nucleolus. The original is in colour. Ehrlich-Biondi staining. (Giuseppe Levi 262.)

horn of the spinal cord, for example, they are constantly semilunar, delicate and elongated, so that often they embrace the voluminous nucleolus in a green ring. He also describes the somewhat different characters presented by the nuclei of the two varieties of karyochrome nerve-cells; but this subject is more fully dealt with in a later paper (262-263). He has never seen in his preparations the endo-nucleoli to which Lenhossék refers. The accessory nucleoli that have been described evidently correspond to the acidophile granules, some of which, at least, in lower vertebrates, are little inferior in volume to the nucleolus. They differ, however, from the latter in never being surrounded by basophile particles. He maintains that the basophile particles are composed of nuclein (chromatin) and that they constitute the whole of this substance contained in the somatochrome nerve-cells. In the course of his observations upon the fuchsinophile granules of the nerve-cell, he observed (260) that the basophile particles of the nucleoli of the cells of the spinal ganglia are rounded in form in the resting condition and elongated in that of fatigue. This change he attributes to the enlargement of the nucleolus, which occurs in the latter condition, according to the observations of Mann and Lugaro. In his comparative researches upon nerve-cells, of which he published his account in 1897, Levi (262-263) included the study of the characters of the nuclei. He confirms his previous description, more particularly as regards what he terms the "centralisation of the nuclein in the somatochrome cells." He finds that the nuclei of this class of nerve-cells have essentially the same structural features in all the animals he has studied, but describes the various slight differences he has observed. He regards the nuclear membrane as a true membrane and not merely a part of the nuclear stroma, as in neuroglia cells. In mammals the nuclear reticulum, or lining network, is very loose and faintly colourable. While the centralisation of the nuclein is complete in the somatochrome cells of mammals, in all the lower vertebrates, although the greater part of the nuclein is centralised, there is a certain quantity of it diffused throughout the nucleus. The nuclei of the *kernzellen* have a delicate, acidophile membrane. Their nucleoli present many variations. They are very small, generally irregular in outline and always composed of two substances, nuclein and one or two acidophile particles. Centralisation of the nuclein is, as a rule, only partial. In the granules of the cerebellum, &c., it is doubtful if the nuclear membrane is always acidophile. Acidophile substance is always present in the nucleus, but it is very scanty. Chromatin is, on the other hand, abundant. The nuclei of the neuroglia cells have a membrane composed of chromatin and a dense reticulum of the same substance. There is, however, no precise differential criterion by which it is possible to distinguish them from those of the granules.

Van Gehuchten (169) refers to Levi's observations, and gives a description of the nucleus essentially in agreement with his view, except as regards the nucleolus, which he seems to regard as composed entirely of chromatin. Lenhossék (281) confirms Levi's statement that the nuclear reticulum is always acidophile. He doubts, however, if the basophile particles in the nucleolus are a constant morphological feature, and thinks that their basophile character is only relative. As will be seen, he altered this opinion shortly afterwards. Prenant (400) describes the occurrence of crystalloid rods in the nuclei of the nerve-cells of the sympathetic ganglia of the hedgehog. They are straight or curved, generally long and intensely coloured.

In 1898 Bühler (41) distinguished in the nucleus of the nerve-cell an acidophile chromatin and a basophile; the first (oxychromatin) is much more abundant than the second. The nucleolus is composed of a substance very nearly allied to basi-chromatin but not identical with it. He did not refer to the special disposition of the nuclein described by Levi. Heimann (210) states that the nucleolus presents a resistance to stains similar to that exhibited by bacterial spores. He regards the nuclear reticulum as basophile (211). Lenhossék (282) considers that the terms acidophile and basophile should not be used in too absolute a sense with regard to the staining reactions of the constituents of the nucleus and nucleolus. He regards it as settled that the nuclear reticulum of nerve-cells has only a very faint affinity for basic dyes, and that on the other hand it colours intensely with acid dyes. With regard to the nucleolus he now accepts the views of Levi.

It should be mentioned here that Goldscheider and Flatau (167), in a work which has probably been widely read in this country, gave an erroneous account of Levi's conclusions regarding the structure of the nucleus of the nerve-cell. Ewing (135) has also fallen into an error in his reference to Levi's description of the changes that occur in the basophile particles of the nucleoli of the cells of the spinal ganglia after prolonged stimulation of the sciatic, attributing to him the belief "that during cellular activity there is an increase in the size and number of the granules of true chromatin lying about the nucleoli of these cells."

Timofeew (506) states that the nuclei of the nerve-cells of birds have two nucleoli, one of which has the characters described by Levi, while the other is entirely acidophile.

In his latest paper on the subject of the nucleus, Levi (265) reviews the recent observations recorded by other authorities, and defends his opinions against certain criticisms that have been offered. He refers to the fact that his statement that the nuclear membrane of the large nerve-cells is always acidophile in reaction has been confirmed by Lenhossék (282), Ramon y Cajal (426) and van Gehuchten (169). He especially criticises the conclusions of Bühler (41), which differ essentially from his own. He maintains his statement that the basophile character of the nucleolar particles is absolute, and disputes the opinion of Ramon y Cajal (426) that the whole of the nucleolus is composed of chromatin, insisting on the acidophile character of the central portion.

(9) *Mode of Connection of Nerve-Cells.*

According to the neuron theory, every nerve-cell with its protoplasmic processes, axis-cylinder process and collaterals, is an anatomical unit, structurally independent of other nerve-cells; the nerve wave passes from one cell to another by way of contiguous terminal arborisations of axis-cylinder processes and protoplasmic processes or nerve-cell bodies, never by anastomosing branches; neither the network of Gerlach, formed by anastomoses of protoplasmic processes of adjacent cells, nor the diffuse network of Golgi, formed by the branches of adjacent axis-cylinder processes, have any real existence. The neuron theory has, however, always had its opponents, and at the present moment a most serious attempt is being made to entirely overthrow it. The evidence that had been adduced against it up to 1894 has been very clearly stated by Tanzi (499), and van Gehuchten (168), in the last edition of his text-book, gives an excellent historical account of the whole matter up till 1896. I shall notice here only some of the more recent observations that have been recorded in support of the existence of direct connections. In 1893 Dogiel (115) described in the retina various forms of anastomoses between nerve-cells. An excellent *résumé* of his views, as well as of those of others who have recently studied the cells of the same organ, will be found in van Gehuchten's book. Ramon y Cajal (428) and many other authorities deny the existence of anastomoses in the retina, while some observers (Renaut, 451, Bouin, 64, &c.) describe anastomoses of a different kind from those of Dogiel. In 1895 Golgi (158), in a paper upon the foot of the hippocampus, defended his views regarding the existence of a diffuse nervous network. In the same year Vassale and Donaggio (515) stated that in the cerebral cortex they had observed by means of a new chrome silver method appearances pointing to the existence of anastomoses between the gemmulae of the protoplasmic processes of nerve-cells and the fine ramifications of the axis-cylinder processes of other cells.

In 1896 Hill (204) from observations by the chrome silver method was led to regard it as at least possible that the thorns of the protoplasmic processes of the cells of Purkinje may contain the ends of the axis-cylinder processes of the granules.

In 1897 Held (202) stated that he had observed in the adult a true concrescence, a relation of continuity and not simply one of contiguity, between the terminations of a branch of an axis-cylinder process, on the one hand, and the cell-body or protoplasmic process of another cell, on the other. He did not, however, consider that the existence of this relation disproves the doctrine of the neuron. In a later paper (203) he maintained that nerve-cells have two modes of direct union; firstly, that just referred to, and secondly by the branches of their axis-cylinder processes which terminate in a common pericellular network around another cell. In this year (1897) Apáthy (8) published an account of his remarkable observations upon the structure of the nervous system which constitute by far the most weighty evidence that has yet been advanced against the neuron theory. I have not had access to Apáthy's monograph, and know of his views chiefly through the very full *recensione* that has been given of it by Levi (268), and the critical paper of Barker (62). The following is a translation of Levi's review in so far as it relates to the subject of this subsection: "In this work of more than two hundred pages, with nine plates, the author describes the results of more than ten years of research, results which until now he has communicated only very summarily in short notes. The author promises to follow this paper with another, in which will be discussed the observations of preceding authors. He made his observations upon the central and peripheral nervous system of leeches and earthworms, and of certain vertebrates. The methods of technique adopted were the following:—Vital colouration by methylene blue; colouration in mass (of pieces fixed in sublimate) with hæmatein Ia; chloride of gold, making it act either upon fresh pieces, or upon pieces fixed in sublimate, or in other ways. The fundamental idea upon which the whole work is based is this: The nervous system is constituted by two kinds of very different cellular elements, nerve-cells and ganglion cells. The first differentiate in ontogenetic development into conducting substance, into primitive fibrils; the second become adult ganglion cells, and are united by the fibrils. The paths which in the adult are traversed by the fibrils are already traced out at an early period of development, and are represented by intercellular bridges. None of his methods, however, permit of the establishment of the precise moment at which the conducting substance is formed. The anatomical unit, truly specific of the conducting substance, is thus the primitive fibril, or neuro-fibril, which pursues uninterruptedly a very long course from the sensory cell, from which it originates, to the ganglion-cell, which it traverses, and from there it passes to a second and to a third ganglion cell, and then enters a muscular fibre. The neuro-fibril (*primitivfibrille*) is constituted by *elementarfibrillen* which are recognisable only when the fibril branches either in a ganglion-cell or in a termination; when this occurs it breaks up into its elementary constituents which, however, can unite again and form the continuation of the neuro-fibril. Between the neuro-fibrils there are very numerous anastomoses, represented, however, at least in the nerve-centres, by very delicate fibrils, which are destroyed in Golgi's preparations. Thus it is to be explained why hitherto the existence of such anastomoses has been denied. But not only between the peripheral fibres but also between the ganglion-cells there are anastomoses (cellular bridges). Another mode of union occurs by two ganglion-cells sending their axis-cylinder processes into the same nerve-fibre. The author, it will be seen, believes that he has demonstrated with facts what Gerlach advanced only as a hypothesis. He maintains that his fundamental law of the continuity of neuro-fibrils can be demonstrated also in vertebrate animals."

Levi appends to his *recensione* some words of criticism both of these views and of the description given of the internal structure of the ganglion-cells. He thinks that Apáthy's observations on these subjects do not differ much from those made recently on the structure of the nerve-cell of the vertebrates. The great difference consists in the inductions. The impression is aroused by the whole work that the author has wished to make these inductions uniform with a scheme. Certainly his observations often do not justify them.

The bearing of Apáthy's observations upon the neuron theory is dealt with in another section (IV. 1).

Blanes (52) concludes against the opinion of Golgi and Monti that a nervous reticulum formed by the collaterals of certain cells can be demonstrated in the olfactory bulb.

The numerous observations that have been made of the occurrence of twin cells and cells with lobes united to a central portion by means of fibrillar bridges, need scarcely detain us here (see Rossi (437), Pugnat (393), Levi (262), Marinesco (322), van Gehuchten (168)). In some instances they are to be explained as arrests of development, in others they appear to represent an exceptional but still normal condition in the adult, but in no case does their existence really affect the neuron theory. Capobianco and Fragnito (87) have recently maintained that direct connection of nerve-cells by their protoplasmic prolongations is a common histological feature, although one that does not readily admit of demonstration. They think that it cannot be explained as an error of development.

Semi Meyer (346) has observed a new mode of connection of neurons in the nucleus of the sixth nerve, consisting in the termination of certain axis-cylinders in spherical or elongated swellings which rest upon the bodies of the nerve-cells. L. Auerbach (10-11) has recently, with the aid of a new staining method, observed that the nerve-fibres which terminate around a nerve-cell are not independent of each other, but form a close network running parallel to the cellular surface. From this network short fibrils are given off which terminate upon the cell by little thickenings. They do not, however, establish any true continuity with the fibrils of the cell.

(10) *Morphological Classification of Nerve-cells.*

In 1894 Nissl (363) maintained that the various arrangements presented by the chromatic substance in the protoplasm of the nerve-cells of the central nervous system permits of the distinction of different types of cell. In the following year (365) he developed this idea further, and gave an elaborate classification of nerve-cells according to their morphology. He divided them into :—

(*a*) Cytochrome nerve-cells, or granules.
(*b*) Karyochrome nerve-cells, or nuclear cells.
(*c*) Somatochrome nerve-cells, or cell-body cells.

The cytochrome nerve-cells are small elements which present only a nucleus, the protoplasm being indistinguishable (in preparations by Nissl's method). The nerve-cells of the granular layer of the cerebellum are an example of this class.

The karyochrome nerve-cells differ from the preceding only in the larger size of their nucleus. Examples are seen in the cells of the *substantia gelatinosa* of Rolando.

The somatochrome nerve-cells have a cell-body which completely surrounds the nucleus, has a distinct outline and contains a stainable substance.

Virtually there are only two classes—the somatochrome and the karyochrome—the cytochrome cells being merely a variety of the latter.

Nissl divides the somatochrome cells into four groups, each of which again he divides into various types. The four groups are as follows:—

(1) *Arkyochrome nerve-cells.*—The colourable constituent is arranged in the form of a net-work.

(2) *Stichochrome nerve-cells.*—The colourable constituent is arranged in the form of parallel bands (motor cells, etc.).

(3) *Arkyostichochrome nerve-cells.*—The arrangement of a net-work and of parallel bands is combined. (Cells of Purkinje, etc.)

(4) *Gryochrome nerve-cells.*—The colourable constituent consists of small granules.

It is scarcely necessary to enter into the further details of this classification here. It has been much criticised, and little of it except its broad distinction of somatochrome and karyochrome nerve-cells is now in general use.

Van Gehuchten (168) thinks that the distinction between karyochrome and cytochrome cells is not justified, and that the division of somatochrome cells into different groups according to the special disposition of the chromatic substance has as yet only an exceedingly limited value. Colucci (88) thinks that the view of the nerve-cells obtained by Nissl's method is too one-sided to allow of a classification being based upon it. Levi (262) thinks that nerve-cells have as yet been too little studied to permit of a morphological classification of them. In his description of the results of his comparative researches he retains the classification of Nissl merely for convenience, stating at the same time that the criteria of his distinctions are different from those of Nissl. Marinesco (314) has justly remarked that a rational classification of nerve-cells ought not to neglect either of the two organized elements of the cytoplasm. A classification having for its basis the chromophile elements alone is incomplete. *Goldscheider and Flatau* (167), on the other hand, think that Nissl's classification is not yet sufficiently valued.

(11) *Structural Changes accompanying Modifications of Functional State.*

I shall deal here only with observations upon structural changes in the strict sense, leaving the subject of alterations in the form of the nerve-cell (amœboidism or plasticity) to be considered in a later section.

The observations of Hodge in this field, as well as those of the next two writers mentioned, do not fall within the period under review, but as they require to be compared with later work I notice them briefly here.

In 1889 Hodge (196) described the changes produced in the sympathetic ganglia of frogs and cats by electrical stimulation of a nerve going to one or more of these ganglia. He found in the nucleus decrease in size, irregularity of outline, loss of open reticular appearance, darker staining; in the protoplasm, slight shrinkage, diminution of power to stain or to reduce osmic acid, vacuolation; in the cell-capsule, decrease in the size of the nuclei. In 1892 he described the following changes as produced in the spinal ganglia and brain of birds by fatigue (197):—Diminution in size of nucleus, irregularity and jaggedness of its outline, darker staining of its reticulum, shrinkage of the cell-protoplasm, vacuolation (spinal ganglia), and enlargement of pericellular spaces. In 1892 Vas (510) found that stimulation of the cervical sympathetic of the rabbit for fifteen minutes at a definite distance from the superior cervical ganglion, produced the following changes in the nerve-cells of this ganglion :—Increase in size of cell-body and nucleus, loss of chromatic substance around the nucleus and increase of it at the periphery of the cell, suggesting movement of the granules to the periphery. Lambert (289) repeated the experiments of Vas and confirmed his conclusions, except as regards the increase in the size of the cells and their nuclei.

In 1894 G. Mann (330) published an account of his now well-known series of observations. He commenced by repeating the experiments of Vas, employing, however, a special histological technique of his own in which was included staining with methyl blue and eosine and with toluidin blue. He concluded that an increase in the size of the ganglion cells and their nuclei does take place, but he could not convince himself of a shifting of the granules from the centre towards the periphery of the cell. The centre certainly became clearer, but this was to be attributed to other causes. He observed also an increased affinity of the nuclear hyaloplasm for eosine and slight diminution of the nuclear chromatin (instead of an increase as described by Vas). The nucleolus enlarged and became at the same time paler. After prolonged stimulation the nuclei began to darken slightly and to shrivel, and the chromatic substance of the protoplasm was greatly diminished. Even in extreme fatigue, however, he did not find that the nuclei were darker than the protoplasm. He also studied the cells of the motor cortex and spinal cord of fatigued dogs. In the cortex there was great diminution of the chromatic substance of the protoplasm, swelling of the nucleus and pallor of the nuclear hyaloplasm; in the cord (lumbar region) the chromatic substance of the protoplasm was diminished in amount and pale, the nucleus was darker than the protoplasm instead of lighter, and at the same time homogeneous and shrivelled. In the retina of the dog fatigued by prolonged exposure to light, as well as in the centres connected therewith, he also observed distinct structural changes. He summed up the conclusions derived from all these observations as follows :—

During rest several chromatic materials are stored up in the nerve-cell, and these materials are used up by it during the performance of its function; activity is accompanied by an increase in the size of the cells, nuclei and nucleoli of the sympathetic, ordinary motor and sensory ganglion cells; fatigue of the nerve-cell is accompanied by shrivelling of the nucleus, and probably also of the cell, and by the formation of a diffuse chromatic material in the nucleus.

In 1895 Lugaro (238) made his important contribution to our knowledge of this subject. He reviewed the observations already recorded, and pointed out their contradictory character. He maintained that the method of experimentation of Vas could not be regarded as furnishing a comparison between the condition of repose and that of activity. On the one hand the cells of the sympathetic ganglion were in a state of normal activity, in the other they had been for a short time over-excited, or had suffered an abnormal form of excitement. His own experiments consisted of variations upon those of Vas. To secure cells in a state of rest he killed animals rapidly under chloroform, and allowed the ganglia to remain for some hours *in situ* before fixing. He confirmed the conclusion of Nissl that the chromophile state of the nerve-cell is an artificial condition, and suggested that it is produced by the sudden action of alcohol. He could not observe the changes in the chromatic substance of the protoplasm described by Vas. Variations in the quantity of this substance in different states were only very slight, and were "subject to the incertitude of subjective appreciations." Differences of chromatic intensity in the cells of the same ganglion certainly could not be exclusively attributed to differences in functional state. Even in ganglia which had been long stimulated, there could always be distinguished clear cells and dark cells, with all intermediate gradations. He summed up his conclusions as follows:—(1) Activity of the nerve-cell is accompanied by swelling of the protoplasm of the cell-body; (2) fatigue produces a progressive diminution in the size of the cell-body; (3) in moderate degrees of activity, while the protoplasm of the cell-body is swollen, the nucleus does not undergo any change in size; (4) when activity is continuous and long protracted, the nucleus undergoes modifications analogous to those of the cell-body, but less intense; (5) the quantity of the chromatic substance in the cell-body varies especially as an individual character in relation to the size; nevertheless it is probable that the first phases of activity determine a slight increase in it, the later phases, accompanied by fatigue, a diminution and a more diffuse distribution; (6) activity of the cell determines in the nucleoli an increase of volume which gives way slowly to the reducing action of fatigue. In the same year Nissl (370) made a long communication upon this subject, in which he severely criticised most of the conclusions previously recorded. Two years before he had maintained that the different degrees of affinity presented by nerve-cells for basic stains, or differences in quantity of chromatic substance in the protoplasm, were probably due to the diverse functional states of activity and repose (360). In another paper (365), published early in 1895, he distinguished these different degrees of colourability by the terms *pycnomorphous*, *parapycnomorphous* and *apycnomorphous*, applying the first to cells which stained very deeply, the third to those which stained very faintly, and the second to those which showed an intermediate intensity of colour. He stimulated the facial nerve with the faradic current, and observed that there was afterwards a preponderance of dark cells in the nucleus of origin. He concluded that the pycnomorphous condition (which is to be distinguished from the artificially produced chromophile state in which the cell is still more deeply and very diffusely stained) represents a state of fatigue in the cell, and that the apycnomorphous condition represents a state of relative repose. Thus he believed, contrarily to Mann, that the chromatic substance accumulates in the cell during its functional activity. In his paper (370) dealing specially with this subject, however, he admits that the pycnomorphous condition must be regarded as the anatomical expression of the resting state. But he maintains that the conditions which Hodge and Mann believed to be characteristic of fatigue and exhaustion are artificially produced, and that the anatomical conditions characteristic of these states still require to be determined. He thinks that faradic stimulation should not be used in such experiments, as it gives rise to changes which are to be attributed to chemical, thermic and traumatic irritations.

In 1896 Valenza (512) described the results of experiments upon the electric lobe of the triton. He found that direct stimulation by strong faradic currents caused a hyperchromatosis of the nuclei of the nerve-cells, accompanied in the slighter degrees by swelling, in the more severe degrees by contraction. Fatigue produced by currents of medium force never caused any alteration in the volume of the cells, of their nuclei or nucleoli. Eve (136) repeated the experiments upon the cervical sympathetic ganglia, and also made a series of control experiments. He found that rest and activity caused very little difference in the histological appearances of sympathetic nerve-cells. The only change that he could detect as the result of protracted activity was the occurrence of a slight diffuse blue staining of the cell-substance. His control experiments led him to attribute this diffuse staining to the formation of an acid in the cell and a consequent slight solution and diffusion of the basophile material. Pergens (412-413) found that in the retina of fishes the action of light caused diminution of the chromatic substance in all the strata below the molecular.

In 1898 Pugnat (394-395), from experiments (electrical stimulation) upon the spinal ganglia of kittens, concluded that activity of the nerve-cell is accompanied by increase in the volume of the cell-body and nucleus, and by diminution of the chromatic substance of the protoplasm, and fatigue by diminution of the cell and of its nucleus, and decrease in the amount of chromatic substance. F. Pick (401) stimulated the motor cortex of monkeys and cats with the faradic current in such a way as to cause unilateral contractions, thus producing fatigue of the motor cells of the cord on one side only. He found that in the fatigued cells the chromatic substance of the protoplasm was diminished and broken up into fine granules, which were placed mostly at the periphery of the cell. The nuclei were shrunken. Luxenburg (276) obtained results very similar to those of Pick by stimulation of a crural nerve after hemisection of the cord and transverse section at a higher level. G. P. Pellizzi (410) has endeavoured to study the process of atrophy from suspension of function while the nutrition of the nerve-cells is preserved, by isolating a portion of the frontal lobe in dogs without severing the essential vascular connections. He finds that the cell-body undergoes a progressive atrophy which slowly extends centrifugally to the protoplasmic prolongations, which for a long time maintain their normal characters. The chromatic substance of the protoplasm is preserved until the atrophy of the cell is advanced. In a later paper (411) he records some very important observations upon the cells of the cœliac and mesenteric ganglia in dogs during the different stages of digestion, from which he concludes that the chromatic particles of the protoplasm become consumed during functional activity of the cell.

Giuseppe Levi (260) has studied this question from a different point of view from that of the observers already mentioned. He endeavoured to investigate by a micro-chemical analysis the intra-cellular products of the metabolism of the nerve-cell, and to study the qualitative and quantative modifications of these during the functional states, as had previously been done in the case of certain other tissues. His researches were made upon the 7th lumbar ganglion of rabbits. Activity was produced in the cells by faradic stimulation of the sciatic nerve. He used Hermann's solution for fixation of the tissues, and stained by Galeotti's acid fuchsine and methyl green method. These observations led to the discovery of the fuchsinophile granules of the nerve-cell, which Levi regards as a true product of metabolism. They are present in the normal cell and consist of exceedingly minute particles which are sometimes slightly elongated. They are coloured bright red by the above staining method, thus contrasting sharply with the other elements of the cell, which are stained green. They lie in the interfibrillar, unorganised substance of the protoplasm, but occur also, though only in small numbers, in the nucleus. In the resting condition of the cells (attained by section of the sciatic nerve and examination of the ganglion after two days) these granules were diminished in numbers. On the other hand, after stimulation of the nerve they were greatly increased in numbers and in size, many of them appearing considerably elongated. The maximum was reached after stimulation for about two hours.

Levi (266) has recently made another valuable contribution to our knowledge of this subject, consisting of a study of the changes occurring in the nerve-cells of cold-blooded animals during hibernation. It has been observed by himself and Jacobsohn (223) that there are no appreciable structural modifications of the nerve-cells of warm-blooded animals associated with this state. Bühler (41), in his work on the nerve-cell, which was published shortly before Levi's paper, described certain special appearances in fresh sections of the spinal ganglia of the hibernating frog, but he did not record any observations of changes recognisable in preparations fixed and stained. Levi's studies were made chiefly upon the cells of the spinal cord and spinal ganglia of the toad. His main conclusions are as follows:—The chromophile substance diminishes greatly during hibernation; in the spinal ganglia it at the same time becomes strongly basophile; it gradually increases when hibernation terminates; during hibernation droplets of fat are present in the cytoplasm, and the interfibrillar fuchsinophile granules are diminished. He concludes, after considering the question from many points of view, that these morphological changes can only be regarded as an expression of the difference in the quantity of the functional energy that the nerve-cells are capable of displaying in the hibernating state, the great diminution of the chromophile substance corresponding to the torpor and diminished excitability of the animals during winter, its increase to the vivacity which they exhibit in spring and summer.

(12) *Physiological Regressive Changes.*

Granting that senility may be regarded as a physiological condition, there are certain nerve-cell changes constantly associated with it which we may perhaps correctly designate by the above title. Hodge (198) studied these changes in man and the bee, and observed not only alterations in the nucleus and pigmentation and vacuolation of the protoplasm, but also a complete disappearance of a large percentage of the cells. Pugnat (397), who supports the views of Hodge, has observed in the spinal ganglia of aged animals nerve-cells profoundly altered and invaded by leucocytes. The writer and Orr (457) have described the changes observed in the cortical nerve-cells in a case of apparently uncomplicated senility in a woman aged 90. Most of the cells showed a large collection of yellow pigment in their interior, often replacing the greater part of the protoplasm. A large proportion of these cells appeared in other respects perfectly healthy, showing very clearly marked and abundant Nissl-bodies in the remaining protoplasm, and a normal number of processes. Very many of them, however, showed further changes of a disintegrative character, consisting in progressive atrophy of the protoplasmic processes, shrinkage of the cell-body and loss of its angular form, disintegration of the Nissl-bodies, and loss of their affinity for basic dyes, and disintegration of the nucleus. Finally there were left only a few stained granules representing the remains of the nucleus and Nissl-bodies, accompanied generally by some scattered granules of yellow pigment.

Many other writers refer incidentally to the pigmentary and other changes that occur in the nerve-cells in senility, but a systematic histological research upon the subject is apparently still needed.

It seems very probable that these regressive changes, which are typically seen in senility, occur to a slight extent throughout life, increasing as age advances. There seems at least to be at present no other hypothesis that will explain the presence of the occasional disintegrating cell that may be found in even the healthiest brain obtained under the most favourable conditions. Luzenberger (285) observed in the cerebral cortex of the guinea-pig cells of this nature in very limited numbers surrounded by quite normal cells. He concluded that their occurrence could not be accounted for by defects of *technique*, and that it could only be explained by supposing that in normal conditions a certain number of cells are in a regressive phase which ends in complete destruction. He described this "involution of normal life" as consisting in the homogeneous rarification of the cell with destruction of the nucleus. The writer and Orr (457) from their own observations have supported Luzenberger's hypothesis and insisted upon its practical importance. It would seem that even in the healthiest nerve-cell community there are some sickly individuals,—cells which from some cause, hereditary or acquired, have become unable to maintain a normal correspondence with their environment.

Marinesco (327) has recently expressed the opinion that nerve-cells, like all other cells, undergo, in proportion as the individual advances in age, a process of involution which causes the chromatophile elements to become reduced in volume and even to assume a powdery appearance.

(13) *Structural Features of the Nerve-Cells of different parts of the Central Nervous System.*

I shall here merely enumerate the more important references and give an abstract of the description given by the writer who seems to be the best authority upon each set of nerve-cells.

Nerve-cells of the spinal ganglia.—The structural features of these cells have been specially described by Flemming (139-140-142), Nissl (360), Dogiel (118), R. A. Fleming (145), Lugaro (244-245-253), van Gehuchten (168-169), Levi (262), van Gehuchten and Nélis (176), Ramon y Cajal (436-434), Lenhossék (281-282), Huber (212), W. H. Cox (94-95-96), Heimann (210-211). I select the description given by Lugaro. He distinguishes in the spinal ganglia of the dog five types of nerve-cell:—(1) *Clear cells of large size with small, often granular chromatic particles*, which are scattered throughout the protoplasm, but which are slightly more abundant near the periphery internal to a narrow limiting zone almost deprived of them, sometimes also more abundant near the nucleus. The nucleus is large and clear, and has almost always only one nucleolus. Around the nucleus there is always a narrow achromatic zone. These cells are fairly numerous. (2) *Clear cells of large or medium size, with chromatic particles of irregular form, small and dense,* but larger near the periphery below an achromatic limiting zone. In these cells, as also in those of the preceding type, but in a much clearer manner, it may be observed that the single particles are connected with each other by delicate processes. The nucleus has the same characters as in the first type. These cells are the most numerous of all. (3) *Dark cells of small size with small and dense chromatic particles,* which, however, are larger around the nucleus with which they may be in contact. The clearer part of the protoplasm colours diffusely. The nucleus is diffusely coloured and contains often two or more nucleoli. These cells are somewhat numerous. (4) *Clear cells of small or medium size with very large chromatic particles,* which are small in number and confluent by means of more or less delicate processes. There is often more than one nucleolus. These cells are not numerous. (5) *Clear cells of large size, with long and coherent chromatic particles* which are confluent with each other and disposed in layers arranged concentrically around the nucleus. These cells are the least numerous of all.

Lugaro's views with regard to the arrangement of the fibrillar part of these cells have already been stated [I. 3].

Cells of the columns of Clarke.—Marinesco (306) has briefly drawn attention to the peculiar characters presented by these cells. Many of them show a peripheral disposition of the nucleus and chromatic elements confined to a peripheral ring.

The normal structural features of these cells require further investigation. Numerous instances might be cited here in which they have been described as morbid changes.

Nerve-cells of the sympathetic ganglia.—These have been recently described especially by G. Mann (330), Dogiel (116), Apolant (14), Juschtschenko (224), Eve (136), Marina (351), Brukner (65), and Marinesco (322). I take the description given by Marinesco.

The achromatic fundamental substance, or trophoplasm, is remarkable in that it presents a variable colourability, in some instances staining in an intense manner with basic dyes, in others remaining quite colourless. The achromatic organised substance, or spongioplasm, is in the form of a network as in other nerve-cells. The meshes of this network may be wide or narrow. The chromatic substance of the protoplasm in a very large number of the cells is developed only at the periphery, leaving a more or less clear perinuclear zone. It has a granular aspect. A second type of cell occurs especially in the superior cervical ganglion. The chromatic granules are placed around the nucleus, while at the periphery of the protoplasm they are entirely absent. In a third type the chromatic elements are disseminated throughout the protoplasm, or arranged concentrically. A fourth type is constituted by certain twin cells (*cellules-jumelles*) which occur especially in the inferior cervical ganglion. They are sister cells placed in one capsule. They may be joined at one extremity, though only exceptionally. They generally differ considerably in size and in appearance.

The nerve-cells of the brain and those of the anterior and posterior horns of the spinal cord, scarcely call for special notice here, as there is probably little that could be added to the descriptions of them that may be found in the text-books already mentioned. Two excellent studies of the cells of the normal cerebral cortex will be found in the papers of Hammarberg (200) and Schlapp (488).

II. EXPERIMENTAL PATHOLOGY OF THE NERVE-CELL.

(1) *Changes following Section of the Prolongations.*

Nissl (358), in the communication in which he first described his methylene blue method, gave an account of certain changes which he had been able to observe by means of this method in the facial nucleus of the rabbit after eruption of the nerve. The report above referred to was published in 1892, but the communication itself is stated to have been made in 1890. The morbid changes, which could be seen in the cells within twenty-four hours, consisted in breaking down and disappearance of the chromatin-bodies, beginning at a particular part of the cell. In two or three days they had proceeded much further, extending over the whole cell. About the third day the protoplasmic processes became involved, showing shrinkage and loss of their chromatin striation. By the fourth day there was a swelling of the whole cell, the contour of which at the same time often appeared as if corroded. Later the cell appeared very pale and finely granular, and the nucleus moved to the periphery, sometimes projecting from the cell-body. All the cells of the nucleus were not equally affected. Many normal cells remained beside the degenerated ones. In 1894 Nissl (362) published an account of further observations of the same kind, and described the procedure by which the lesions were produced as a new method of experimental research for the nervous system by means of which it was possible to localise the various nerve-centres. He proposed to designate this method *the method of primary irritation*. His experiments were made upon the facial and other cranial nerves, and also upon some of the peripheral nerves. The changes described were essentially similar to those just detailed. He believed that the changes were the same whether the nerve was cut, excised or torn out, the essential thing being complete and continued interruption of the connection between the nerve and its centre. They reached their height in from eighteen to thirty days. After this they were stationary for a time, and then began to be repaired. In fifty or sixty days after rupture of the facial nerve the cells that had been affected could scarcely be distinguished. Individual nerve-centres showed considerable differences in their mode of reaction.

In 1895 Vanlair (516), from the results of a series of experiments upon dogs, concluded that division of a spinal nerve is in no case followed by any alterations in the structure of the spinal cord. His examinations were made from six months to two and a half years after the operation. Later in the same year Onuf (386) published an account of his experimental investigations. His paper contains a valuable *résumé* of previous observations of a similar kind, which, however, were mostly carried out with unsuitable staining methods. He states that his own observations were made before he knew of Nissl's work on the same subject. His experiments were made upon cats, in which he cut the anterior roots (sometimes also the posterior) of spinal nerves. He secured the cord in from three days to four weeks afterwards. He used chiefly a modification of Nissl's older magenta method. The results of his independent observations agree essentially with those of Nissl. He found that in a large number of the multipolar cells of the anterior horn connected with a cut anterior nerve-root, and also in some in the opposite anterior horn, the differentiation of the chromatophile and chromatophobe substance of the cell-body was lost, and that an appearance was produced corresponding to that described by Friedmann as "homogeneous swelling." He observed that this change began in a circumscribed portion of the protoplasm, and gradually extended to the cell-body and its processes, and that the nucleus became dislocated towards the periphery. He believed that the affected cells became completely destroyed. He described this as an acute change, which generally followed section of the nerve near the cell. He distinguished also a gradual change in which the cell assumed an appearance corresponding pretty closely to Nissl's chromophile state. It was generally produced by lesion of a motor fibre at a considerable distance from the cell.

In 1896 Ceni (73) recorded the results of a series of experiments in which he cut the spinal cord of four dogs and examined the cerebral cortex in from 7 to 110 days later. The changes he described may be attributed, in part at least, to section of the prolongations of cortical nerve-cells. He found that in preparations by Golgi's method certain of these cells presented an atrophic and varicose condition commencing at the extremities of the protoplasmic prolongations and extending gradually to the cell-bodies. The nervous prolongations were only affected at a very advanced stage. These changes were not uniformly distributed, but affected individual cells and groups of cells in various portions of the cortex. After hemisection of the cord most of the cells affected were in the cerebral cortex of the opposite side. Marinesco

(305) described the results of his observations upon the nerve-cells of the cord after section of peripheral nerves, confirming most of the conclusions of Nissl and Onuf. He divided the changes in the central-end of the cut nerve and in the cell into two phases. In the first the central end of the nerve remains intact, while in the cell there is produced a *réaction à distance*, characterised by more or less complete dissolution of the chromatic elements of the protoplasm, a morbid change which he here designated *chromatolysis;* in the second there is disintegration of the trophoplasm (a term which at this time he applied to the whole of the achromatic part of the cell) and changes in the central end of the cut nerve. The first is the degeneration of Nissl; the second is the degeneration of Hayem and Forel. These changes differ from Wallerian degeneration which has its seat in the peripheral end of the cut nerve. He was of opinion that some of the affected cells atrophied and disappeared. He further maintained that these changes in the nerve-cell, secondary to injury of its nervous process, have special characters which permit of their distinction from primary lesions, that is to say from those produced by the direct action of a poison.

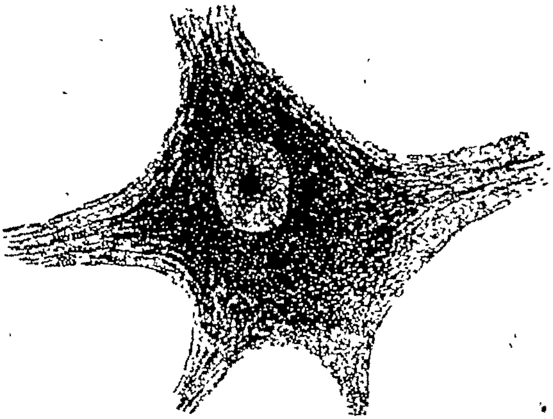

FIG. 10.

Nerve-cell of anterior horn of spinal cord of guinea-pig. Incipient chromatolysis from section of nervous prolongation. Reactive phase. Sublimate. Thionin. Compare with Fig. 1. (Lugaro 242.)

Lugaro (242) described the results of experiments similar to those of Marinesco. He employed, in addition to thionin staining, the hæmatoxylin methods for the demonstration of the fibrillar portion of the protoplasm. He confirmed the descriptions given by Nissl and Marinesco of the changes in the chromatic part and also the inductions of the latter with regard to the behaviour of the achromatic part. His description of the changes in the large cells of the anterior horn of the spinal cord following section of the sciatic nerve is as follows:—In the first phase of alteration (reactive phase) one observes disintegration of the chromatic part, starting from the origin of the axis-cylinder; the cell otherwise preserves its normal form and the nucleus its position. With hæmatoxylin it can be seen that the achromatic part, in the prolongations and in the cell-body, perfectly preserves its delicate striation, which, indeed, is often rendered more evident by the disintegration of the chromophile particles. In the more advanced stage (degenerative phase) the chromatolysis extends to the greater part of the cell-body, and the nucleus is distinctly displaced. The chromatolysis advances gradually to the protoplasmic processes. In hæmatoxylin preparations the delicate striation has now disappeared from those parts of the cell-body that are most altered, and from the protoplasmic prolongations

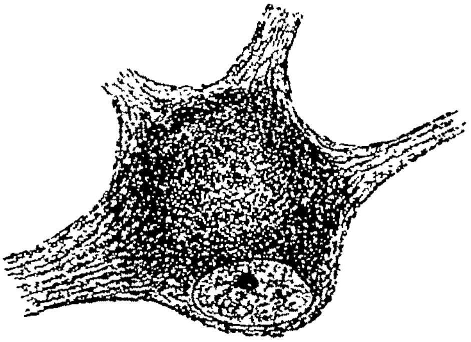

FIG. 11.

Nerve-cell of anterior horn of spinal cord of guinea-pig after section of the nervous prolongation. Initiation of the degenerative phase. Sublimate. Thionin. (Lugaro 242.)

involved in the degenerative process. When the degenerative phase is at its height, the chromatic part appears powdery, and the striation is completely lost. From an examination of the same tissues by Golgi's method, he concluded that it is only with the initiation of the destruction of the cell (degenerative phase) that alterations become recognisable with this method. In this paper he referred, but only very briefly, to the changes that occur in the spinal ganglia after section of the sciatic nerve, stating that his experiments were as yet incomplete. In October of this year R. A. Fleming (143) published an account of what appears to have been the first very complete series of observations with Nissl's method upon the changes in the cells of the spinal ganglia following section of the sciatic nerve. The chief points that he was able to establish are as follows:—The cells of the ganglia of the posterior roots undergo distinct changes as the result of nerve section or ligature, and do so at a much earlier period than the multipolar cells of the cord, beginning probably as early as the fourth day, and certainly by the seventh day. In both, one of the first changes to be observed is diminution in the size of the nucleus, sometimes also of the nucleolus; the nucleus frequently takes up an eccentric position. In both, the Nissl-granules are either smaller in size and fewer in number, or they are grouped together in large masses around the nucleus, leaving the periphery of the cell quite clear. The pericellular spaces tend to become enlarged. An actual atrophy of the cell may also occur. In the multipolar cells there is further a later phenomenon, consisting in marked disintegration of the cell-protoplasm. This change follows only at a very late stage in the cells of the spinal ganglia. It is to be noted that these observations were made upon rabbits and dogs. Colenbrander (97) described in the cells of the anterior horn of the cervical cord of the rabbit, after section of the brachial plexus, changes corresponding essentially to those observed at a lower level after section of the sciatic nerve. Lugaro (243) described his important observations upon the effects of partial mutilation of the nervous prolongations. The conditions necessary for this study he realised by section of the spinal cord at the junction of the dorsal and lumbar portions. It is almost impossible to epitomise the conclusions of this paper. It can only be said here that chromatolytic lesions of various degrees of intensity were found above and below the point of section, and that their localisation was such as to suggest many valuable deductions regarding the connections and distribution of the various groups of cells. It should be mentioned also that the changes found in the cells of the cerebral cortex were very slight. In December of this year Lugaro (244) published a long account of his observations upon the alterations in the nerve-cells of the spinal ganglia, chiefly of the dog, in consequence of section of the peripheral or central branches of their prolongation. The first experiment consisted in the removal of a portion of skin and examination of the cells of the corresponding spinal ganglia after eighteen days. The greater number showed only more or less advanced chromatolysis, without alteration or displacement of the nucleus. The affected cells were exclusively those of the two types of large clear cell. The next series of experiments consisted in excision of the sciatic nerve at the level of the hip-joint and examination of the spinal ganglia after various periods. After twelve days more than half of the cells were affected by chromatolysis in various degrees. In the most advanced the cell-body was swollen, deformed, pale and filled with powdery remains of the chromatic part, the nucleus shrunken, deformed, displaced and deeply stained. Each kind of cell was affected excepting his fourth type. In a dog killed after thirty-nine days similar changes were observed, but there was an evident diminution in the number of nerve-cells, and a prevalence of healthy cells. In some cells the degenerative process had gone on to complete destruction, in others repair had taken place. In guinea-pigs the changes were found to be more uniform, regular and slow, the degenerative phase not manifesting itself until after the twentieth day. Section of the posterior root between the ganglion and the cord produced no distinct changes in the cells of the ganglion. The results of section of the posterior columns of the cord served to confirm the conclusion that these cells are not morphologically affected by section of the central branch of their prolongation. The author discusses at considerable length the physiological deductions to be drawn from these observations. He concludes that it may be supposed that the sensory element resents specially the suppression of external stimuli, the motor element the suppression of the discharge of the energy which it elaborates.

In 1897 R. A. Fleming (144-145) published further accounts of his observations upon the changes in the nerve-cells of the spinal-cord and root-ganglia after section or ligature of the peripheral nerves. Marinesco (314-315), in the *Rapport* presented to the Congress at Moscow, deals very fully with the subject of secondary lesions of the nerve-cell, comparing the conclusions derived from his own observations with those of Lugaro, with which they are essentially in accord. He distinguishes three phases in the changes that occur in the nerve-cell after section of its axis-cylinder,—the reactive, the degenerative and the reparative. The time of the onset of the reactive phase varies considerably in accordance with certain conditions. After section of the hypoglossal in the rabbit, it could be observed in from two to three days; in the dog only after four or five days. He states that he has observed slight reactive changes in the cells of the spinal ganglia after destruction of the nuclei of the posterior columns and of the neighbouring sensory fibres. He gives a description of the reparative phase as observed in the hypoglossal nucleus of the rabbit after section of the nerve. It may be clearly observed in some cells by the twenty-fourth day, when reunion of the ends of the cut nerve commences to take place. The cells undergoing repair are increased in volume, and stain deeply, owing to the density and large volume of the newly-formed chromatophile elements. After forty-six days a greater number of cells have become repaired. There are now no cells in the reactive phase, but there are still many pale degenerated cells. After seventy-three days the density of the chromatic substance, and the volume of the cells undergoing repair are still further increased. After ninety days the hypertrophy of the cells has attained its maximum. After this they diminish in volume, and in an animal killed after 111 days the hypoglossal nuclei of the two sides are indistinguishable from each other. The rapidity of the repair depends chiefly upon two factors,—the age of the animal (being more rapid in young animals) and the union of the two cut ends of the nerve. If union does not take place the number of cells that degenerate and disappear is increased. Van Gehuchten (169), in his paper, likewise communicated to the Moscow congress, gives a very minute description of these changes as observed by himself. He distinguishes two stages in the alterations that occur in the cells of the spinal cord, firstly that of the breaking down of the chromatic particles, and secondly that of their restitution. The first stage is characterised by rapidly spreading destruction of the chromatic elements from the centre to the periphery, increase in volume of the cell and displacement of the nucleus. It begins about forty hours after section of the nerve, quickly attacks simultaneously all the nerve-cells connected therewith, and lasts from fifteen to twenty days. The stage of restitution then begins, in which the chromatic elements slowly form again and the cells exhibit a pycnomorphous condition. His conclusions differ radically from those of Marinesco and Lugaro, for he maintains that the changes observed are due merely to a simple disturbance of the cell which affects exclusively the chromatic substance. In effect he asserts that the occurrence of the degenerative phase has not been proved. He believes that destruction of cells is very slight, and to be attributed when it occurs to loss of the nucleus owing to exaggerated displacement from swelling of the cell. He states that in the cells of the spinal ganglia, on the other hand, reorganisation of the cell does not occur, but complete degeneration and destruction of it. He attributes this difference between the behaviour of the sensory cell and that of the motor cell to the fact that the former is deprived of the trophic influence exercised by its physiological excitement, while the latter is not. In a later paper (170) he expresses similar opinions. He also states that he and Nélis have confirmed Lugaro's observation that the cells of the spinal ganglia do not suffer chromatolysis in consequence of section of the central branch of their prolongation. In another paper (171) published in this year his own observations upon the effects of nerve-section are also related. In December of this year Lugaro (248) described the results of a further experimental investigation of the effects of section of the central branch of the prolongation of the cells of the spinal ganglia. He cut the posterior roots of several spinal nerves between the ganglion and the cord in two dogs, and examined the cells of the ganglia after six and twelve months respectively. In both cases the cells were quite normal in appearance. He disputed the opinion of van Gehuchten regarding the exclusive importance that is to be attributed to the trophic action of the stimuli that flow to the cell, and also dissented from the interpretation of the complete destruction of the cells of the anterior horn as a purely accidental result of nerve-section.

After this time numerous papers were published describing researches upon the localisation of nerve-centres by means of the production of secondary chromatolysis. Among these papers there are to be mentioned the following:—Van Gehuchten (172) and Marinesco (319) on the anatomy of the facial nucleus; Marinesco (323) and van Gehuchten and Buck (178) on the motor nuclei of the lumbo-sacral cord; van Gehuchten (175) on the origins of the glosso-pharyngeal and vagus nerves; Marina (351) on the centres for the movements of the pupil; Bunzl-Federn (66) on the origin of the vagus.

Van Gehuchten (173) has recently published an account of some experimental researches the results of which, to a certain extent, contradict previous conclusions of himself and others. He made a large number of observations upon rabbits, cutting various peripheral nerves, and found that in no instance was the lesion followed by chromatolysis in the corresponding cells of the cord. Some of the cells, however, were found to be in a pycnomorphous condition. On the other hand he found that section of the cranial nerves always produced chromatolysis in the cells of their nuclei of origin. He therefore concludes that the motor spinal neurons and the cranial neurons of the rabbit differ in their power of resistance to traumatism of the axon. Marinesco (323), in his paper on the motor nuclei of the spinal cord of the dog and rabbit, refers to these observations made by van Gehuchten. He himself obtained some similar negative results after section of spinal nerves. He therefore tried the effects of excision of a large portion of the brachial plexus and of eruption of nerves. He found that the latter procedure gave a constant, rapid and very distinct reaction in the nerve-cells of the anterior horns. The alteration produced consisted in complete disappearance of the chromatic elements, while the nucleus and nucleolus were also distinctly affected. This condition he designated *achromatosis*, which, however, was not to be regarded as different from chromatolysis, but merely as a specially severe form of it due to the intensity of the traumatism. He confirmed these conclusions by further experiments upon dogs, of which an account is given in another paper (325). In still another paper (324) upon this subject he stated that the repair of nerve-cells affected by chromatolysis after section of a nerve depends upon the restoration of the continuity of the nerve. After resection or eruption of a nerve this continuity being permanently abolished there is atrophy and disappearance of the cells of the nucleus of origin.

Marinesco (322) was unable to find chromatolysis in the cells of the cervical sympathetic ganglia after section of the cervical sympathetic in the dog. D. Mirto (337), however, obtained positive results. He found that after section of the intracranial and carotid branches of the superior cervical ganglion, there was a severe and rapid chromatolysis in the cells of the ganglion, going on to complete disintegration of the chromatic substance. By the twenty-eighth day he observed diminution in the number of cells. After section of the cord (pre-ganglial fibres) the cells of the ganglion also showed chromatolysis, but it was comparatively slight in degree and in certain respects different in character. Marina (351), in his important researches upon the localisation of the centres for the movements of the pupil, found that the quantity of the degenerated cells in the ciliary ganglion was proportional to the extent of the lesions produced in the iris and ciliary processes.

Warrington (522), after section of the anterior roots of spinal nerves, observed in the corresponding cells of the cord changes similar to those found by others after section of the nerve-trunk. In animals killed from ten to twenty-four days after section of posterior roots he found, chiefly on the corresponding side, severe chromatolysis which showed marked limitation to the postero-external group of cells in the anterior horn. He found comparatively very slight changes in the nuclei of origin of the third and seventh cranial nerves after section of the nerves. It is interesting to compare the above observation upon the effects of section of the posterior roots with one made by Lugaro (243). He found that some days after section of the spinal cord at the junction of the dorsal and lumbar portions the cells of the postero-external group were specially (although not exclusively) altered below the lesion, even as far as the *conus medullaris*. On the other hand, at some little distance above the lesion all the cells of the anterior horn were intact. From these observations he drew the conclusion that these altered cells are probably not cells of the anterior root, but neurons of the second order placed on the sensory tract.

W. H. Cox (96) has given a description of the changes found in the cells of the spinal ganglia of the rabbit which differs considerably from that of previous observers. He describes two types of cells each of which becomes modified in a different way. The cells of the first type suffer chromatolysis which is distinguishable after twenty-four hours. Those of the second type are still intact up to the fourth day. Some days later, however, they present agglomeration of the chromatic granules around the nucleus. He believes that the fibrils are never destroyed, and that all the cells ultimately resume their normal structure. Marinesco (326) has recently very fully described the process of repair in the cells of the hypoglossal nucleus of the rabbit after chromatolysis produced by section of the nerve. He confirms and amplifies his previous description (314). Foà (153) concludes that repair can occur in the cells of the hypoglossal nucleus even when the ends of the cut nerve do not unite. All the cells of centre affected do not recover; some always disappear.

(2) *Changes Produced by Various Poisons (including Bacterial Toxines).*

The effects of various poisons upon nerve-cells have recently been studied by a very large number of observers, not only with the aid of Nissl's method and its modifications, but also by Golgi's method, the hæmatoxylin method and others. The earliest observations of this kind conducted with suitable staining methods appear to have been those of Nissl (359) with lead and arsenic, of which an account was published in 1892. The lesions that he observed and described were merely forms of those that are now grouped together under the term chromatolysis. He found that while in poisoning by arsenic the chromatic particles dissolve and become pale by a process of vacuolation which makes them appear riddled with holes, and in consequence broken up, in poisoning by lead there is a progressive diminution of the chromatic particles which at the same time become more homogeneous and of sharper outline. At the same time, in the achromatic part there appear granules which are quite distinct and deeply coloured in lead poisoning, pale and small in poisoning by arsenic (242). K. Schaffer (462) and Golgi (157) were also early investigators in this field.

The subject of the nerve-cell changes produced by the very numerous toxines that have been employed is probably most conveniently arranged under the individual toxines, and I shall therefore deal with it in this way discarding the purely chronological order.

As important papers dealing with the general subject of these changes, the following may be specially referred to:—Lugaro (245-256), Nissl (371-374), Marinesco (314), Goldscheider and Flatau (167), Jacottet (226), Babes (43), Nageotte and Ettlinger (380-381), and Flatau (148).

Nissl (371), on the basis of his more recent extensive investigation upon this subject, maintains that each poison gives rise to special lesions and affects certain kinds of cell to the exclusion of others. Lugaro (245) states that in primary affections of the nerve-cells from toxic action the first to alter is the chromatic part; alteration of the achromatic part follows with a rapidity which varies with the various toxic agents and with the type of cell. Different poisons give in the same cell alterations of different type; so also a given poison in the different categories of cells.

Arsenic.—The changes produced in the nerve-cells by this poison have been described by Nissl (359-371), K. Schäffer (462), Lugaro (245), Marinesco (314-315-316), Jacottet (226), Soukhanhoff (482), and Dexler (133).

Nissl's description has already been noticed. The observations of Lugaro require special reference. He induced slow poisoning with arsenic in two dogs which were killed after forty-three and fifty days respectively. A large number of the cells of the spinal ganglia showed peripheral chromatolysis in various stages. The achromatic fibrils were not affected, excepting at the periphery of some cells in which the morbid changes were very advanced. The chromatic particles in the cells of the anterior horn of the spinal cord appeared riddled with holes, as described by Nissl. Many of these cells were, however, normal. The achromatic part appeared as a rule intact. The small cells of the columns showed an advanced chromatolysis with

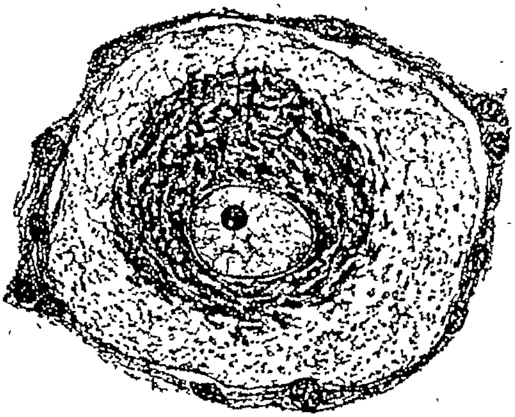

FIG. 12.

Cell of spinal ganglion (dog) showing peripheral chromatolysis. Poisoning with arsenic. Sublimate. Thionin. (Lugaro 245.)

involvement of the achromatic fibrils. In tissues fixed in Flemming's solution some of the degenerated nerve-cells of the spinal ganglia and cord showed fatty granules in their protoplasm. Cox's method showed absence of rosaries on the protoplasmic prolongations and the presence of normal spinous appendages. The cells of the cerebral cortex showed relatively very slight alterations. In Cox preparations they appeared quite normal. In dogs allowed to live for fifty days after the cessation of the administration of arsenic, the cells of the spinal ganglia were mostly normal, but a few showed advanced degenerative changes, apparently having been unable to recover. Marinesco obtained a peripheral chromatolysis in the cells of the spinal ganglia, a more diffuse change in those of the cord.

Lead.—The poisonous effects of the salts of this metal upon nerve-cells have been studied especially by Nissl (359-371), K. Schaffer (462), Lugaro (245), and Jacottet (226).

The observations of Lugaro again demand special note. In the cells of the spinal ganglia of four dogs slowly poisoned with lead acetate, he found, instead of peripheral chromatolysis as in arsenic poisoning, a diffuse disintegration of the chromatic particles and progressive decolourisation of the

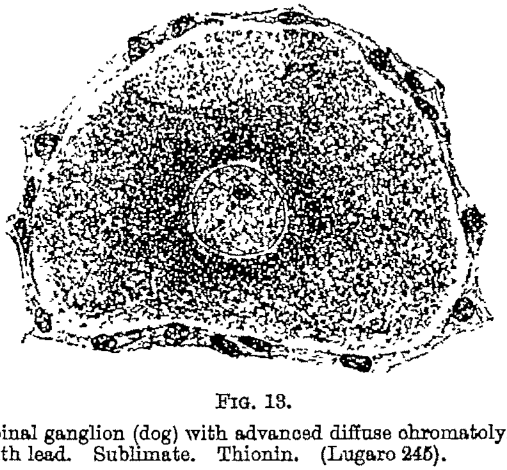

FIG. 13.

Cell of spinal ganglion (dog) with advanced diffuse chromatolysis. Severe poisoning with lead. Sublimate. Thionin. (Lugaro 245).

resulting granules, accompanied by disappearance of the achromatic fibrils. The protoplasm appeared clear, homogeneous and scattered over with extremely fine granules. The nuclei were also more or less distinctly altered. The cells of the cerebral cortex likewise presented these changes, but in a less marked degree. In preparations by Cox's method these cells appeared normal, except in one dog in which the chromatolytic changes were specially pronounced. In this animal many of them presented a condition of varicose atrophy.

Silver Nitrate.—Donaggio (103) has found in dogs killed by administration of large doses of nitrate of silver a peculiar change in the cells of the anterior horns of the spinal cord, more especially in the external and median groups. The chromophile particles of the protoplasmic prolongations were faintly stained, while the body of the cell presented an appearance closely resembling the pycnomorphous condition of Nissl. Many of the other cells of the cord showed advanced chromatolysis. While the cells of the cortex also presented this change, they showed practically no varicose atrophy with Golgi's method.

Phosphorous.—The effects of poisoning by this substance upon nerve-cells have been investigated by Sarbò (484), and more recently by Rossi (439). The latter gave daily injections of solutions of phosphorous in oil to three dogs, producing death in from six to fifteen days. Most of the nerve-cells of the Rolandic area showed only very slight disintegration of the chromatic particles. In some, however, there were more marked changes, in consequence of which they appeared as if broken in pieces, while their cytoplasm contained a powdery detritus. Many of the cells of the cord, more especially those of the anterior horn, showed advanced chromatolysis. It is surprising that this writer makes no reference to the question of the occurrence of fatty changes in the nerve-cells of these animals. In a case of poisoning by phosphorus in the human subject, described by Elkins and Middlemass (137), very decided fatty degeneration was proved to exist in the cortical nerve-cells, involving both protoplasm and nucleus.

Malonnitril.—Goldscheider and Flatau (164-165-167) have observed disintegration of the Nissl-bodies and deep staining of the chromatic substance of the nucleus in the cells of the spinal cord of animals poisoned by this substance. Injection of hyposulphite of soda, by which it is possible to arrest the symptoms of malonnitril poisoning, was followed by restoration of the cells to their normal appearance within three days.

Alcohol.—The changes produced by this substance have been investigated experimentally by Vas (511), Dehio (126), Berkley (22-25-26-27), Marinesco (314-315-316), Jacottet (226), &c.

Dehio observed slight disintegrative changes in the chromatic part of the cytoplasm, and staining of the achromatic part, in many of the cells of Purkinje of rabbits and dogs killed by acute alcoholic poisoning. Berkley (22-27), in chronic alcoholic poisoning in rabbits, observed some dissolution of the Nissl-bodies in the cortical nerve-cells only in the neighbourhood of obstructed vessels. In preparations by his modification of Golgi's silver method he observed marked and widespread changes in the dendrites, consisting of varicosity and atrophy, and structural alterations or complete loss of many of the gemmulæ. Marinesco described various forms of chromatolysis in the cells of the spinal cord in chronic poisoning in the dog. Jacottet observed similar changes in the cells of the cord and spinal ganglia.

Strychnine. — Goldscheider and Flatau (164-166), in poisoning by this substance, found in the nerve-cells of the cord changes similar to those that they have described in experimental tetanus.

Toxine of Tetanus.—The nerve-cell lesions caused by the toxic products of the tetanus bacillus have been studied experimentally by Marinesco (308-314-315), Chantemesse and Marinesco (99), Goldscheider and Flatau (164-166-167), Babes (43), Courmon, Doyen and Paviot (80), Vincenza (509), &c.

Marinesco has observed in some of the nerve-cells of the anterior horn of the spinal cord of guinea-pigs, subjected to the action of tetanic toxine, lesions different in character from any that he has found in other intoxications. The animals were killed some time before death would naturally have supervened, and the cord was removed at once and placed in fixing solution. In guinea-pigs allowed to die from the effects of the toxine the characteristic lesions were not seen. The altered cells show two quite distinct parts. One is darkly and opaquely stained, and its normal structural features are scarcely recognisable. It is placed upon that side of the cell which gives origin to the axis-cylinder process, which itself appears granular and intensely stained. The protoplasmic processes given off from this part show an irregular and even sinuous contour. The other portion of the cell-body preserves an almost normal appearance, as do also the protoplasmic prolongations arising from it. The nucleus is generally enlarged and somewhat diffusely stained. He states that Nissl and Beck have described similar lesions in experimental tetanus. He maintains that it is necessary to distinguish two independent phenomena in nerve-cells subjected to the action of the tetanic poison, one a result of the chemical combination of the poison with the cellular protoplasm, and the other due to the wearing out of the cell from excessive functional activity. He agrees with the conclusion of Goldscheider, that the tetanic poison does not exercise upon the nerve-cell a simple exciting action, but induces a chemical transformation which exalts the excitability of the motor substance. Goldscheider and Flatau give a different description of the changes in experimental tetanus, a fact which is to be accounted for by an essential difference in the mode of experimentation. They state that tetanus poisoning in rabbits causes characteristic changes in the cells of the anterior horns, consisting in an increase in the size of the nucleolus together with pallor of it, increase in size of the Nissl-bodies and crumbling of them, and lastly fine granular disintegration of the Nissl-bodies along with enlargement of the whole cell. They found that the injection of tetanus anti-toxine retarded these cell-changes, and caused a more rapid return to normal.

Chantemesse and Marinesco found that simultaneous injection of tetanus toxine and anti-toxine resulted in no appreciable symptoms, but some modifications were recognisable in the nerve-cells. Courmon, Doyen and Paviot, from experimental results of their own, have endeavoured to discredit the observations of Marinesco, denying that tetanus toxine produces any alterations in the cells of the anterior horns. Vincenza, using Golgi's method, found varicose atrophy of the cells of the cerebral cortex.

Toxine of Rabies.—The nerve-cell changes produced by rabies have been studied experimentally by Golgi (157), Marinesco (314-316) and Caterina (86). In 1894 Golgi described in rabbits inoculated with the virus of rabies, various alterations in the form and structure of the nerve-cells. Some were slightly swollen, transparent and faintly stained. Others presented vacuolation and considerable increase in volume. He also described a vesicular degeneration in which the cell was swollen to several times its normal size; and a granulo-fatty degeneration which presented a very advanced phase of the morbid process. Preparations by his own black reaction method showed progressive atrophic changes beginning in the protoplasmic prolongations and invading the cell-body. Some of the axis-cylinders presented varicose swellings. Marinesco observed severe peripheral chromatolysis and occasional vacuolation in the nerve-cells of the cord of rabbits which had died from rabies. Caterina found similar changes in the guinea-pig.

Toxine of Bubonic Plague.—Lugaro (246) in two rabbits and a guinea-pig killed by inoculation of the virus of bubonic plague found severe chromatolysis of the nerve-cells of the cord and spinal ganglia. The achromatic portion of the protoplasm was affected. The nuclei were shrunken and obscured, presenting the acute homogeneous change described by Sarbò. Babes (42-43) found similar changes in guinea-pigs and mice. He states that the bacilli of plague are occasionally to be observed within the nerve-cells.

Diphtheria Toxine.—In 1895 Crocq (78) described in the nerve-cells of rabbits killed by injections of cultures of Löffler's bacillus changes corresponding to a severe type of chromatolysis. The cells of the anterior horns of the cord were first affected, and afterwards those of the lower part of the medulla oblongata. Ceni (74) described the occurrence of varicose atrophy of the nerve-cells of guinea-pigs and rabbits in experimental diphtheria. Babes (43), who has also studied these changes experimentally, mentions the interesting fact that he has found that the injection of large quantities of diphtheria anti-toxine is capable of producing distinct alterations in the cells of the anterior horn of the spinal cord in rabbits. Mouravieff (348), in guinea-pigs subjected to the action of diphtheria toxine, observed well-marked changes confined to the nerve-cells of the anterior horn of the spinal cord. They consisted of chromatolysis, principally peripheral, vacuolation of the cell-body and its prolongations, a corroded appearance of the edges of the cells, and sometimes loss of the nucleus. In a later paper (349) he described some comparative observations upon the effects of streptococcal infection, and also of the combined action of diphtheritic and streptococcal toxines.

Toxines of Bacillus Botulinus.—Marinesco (310-314-315) has studied the changes produced in the nerve-cells of lower animals by these toxines. He observed severe degrees of chromatolysis, generally commencing peripherally. As the morbid changes advanced there was destruction of the achromatic fibrils and formation of vacuoles. The cells of the spinal cord and medulla oblongata were chiefly affected. Kempner and Pollack (234) have found similar changes in the nerve-cells, and have further observed the slow restoration of the cells to normal under the action of the specific anti-toxine.

The following papers still require mention here:—Müller and Manicatide (352) upon poisoning by acids; Berkley (28) upon ricin poisoning; Pandi (409) and Vas (511) upon poisoning by nicotine, &c.; Daddi (111) and Pandi (409) upon cocaine poisoning; Sarbò (484) and Saratschow (461) upon morphia poisoning; Mourek and Hess (355) upon the effects of numerous different poisons; Koster (235) upon carbon bisulphide poisoning; Borri (63), poisoning by carbonic oxide and by sulphuretted hydrogen; Döllken (132), aluminium; Gabei and Antinori (194), urine, ammonium carbonate, &c.; Crisafulli (83) and Wright (523), potassium bromide; D. Mirto (338), neurine; Brauer (59) and Dotto (128), mercury; D. Mirto (336) *latirismo*.

(3) *Changes produced by other Experimental Lesions.*

Many of the changes dealt with in this subsection (more especially those occurring in inanition, pyrexia, uræmia, and anæmia) are of the greatest practical importance, as they tend to complicate the pathological picture in cases of nervous disease in the human subject, and therefore require to be recognised and discounted before conclusions of any value can be formed regarding the relation of morbid appearances in the nerve-cells to the special clinical symptoms.

Inanition.—The changes in the nerve-cells in this condition have been studied by A. Monti (291-292), Pernice and Scagliosi (406), K. Schaffer (465), Lugaro and Chiozzi (258), Ganfini (186), Daddi (112), and Müller and Manicatide (352).

Monti, using the method of Golgi, observed varicose atrophy of the protoplasmic prolongations. Pernice and Scagliosi observed in fowls deprived of water alone complete disappearance of the chromatic substance and vacuolation; with Golgi's method deformity of the cell-bodies and fragmentation of the dendrites. K. Schaffer observed in the nerve-cells of the cord in rabbits chromatolysis, vacuolation, and the homogeneous change of Sarbò in the nucleus. The lesions were specially severe in animals deprived of water as well as of food. Lugaro and Chiozzi, from observations upon dogs and rabbits killed after various periods of starvation, concluded that the nervous elements remain for a long time intact, or only show slight alterations in the chromatic substance. These alterations are, however, aggravated during the few days preceding death. The achromatic substance and the nucleus may also become involved. Varicose atrophy of the protoplasmic prolongations is always slight, and is not preceded by loss of the spinous processes. They think that the lesions observed are not an expression of atrophy of the nervous elements, but that they are the result of a true auto-intoxication, which becomes rapidly aggravated in the last days of life through simultaneous alterations in the structure of the various viscera. Ganfini found in the rabbit chromatolytic changes in the cells of the cord, but not in those of the cerebral cortex. Daddi has studied the subject in dogs, and obtained results corresponding very closely to those of Lugaro and Chiozzi. He thinks, however, that the changes depend upon general denutrition, and not upon auto-intoxication.

Insomnia.—Daddi (110) in experimental insomnia in dogs found especially in the cortical nerve-cells more or less advanced chromatolysis, swelling of the cell-body, and vacuolation of the protoplasm. The method of Golgi also revealed varicose atrophy of the protoplasmic prolongations and disintegration of the cell-body. The nucleus also presented marked structural changes, and in many instances was displaced to the periphery of the protoplasm. Agostini (1) independently carried out similar experiments and observed practically the same morbid changes.

Ablation of the Supra-renal Bodies.—Ettlinger and Nageotte (379) observed in dogs subjected to this experimental lesion advanced chromatolysis and formation of fissures in the nerve-cells of the cord. Similar, but less pronounced changes were found in the cells of the cerebral cortex. Donetti (113) in rabbits and guinea-pigs found this lesion followed by peripheral and concentric chromatolysis, going on frequently to complete destruction of the cells. The changes were most advanced in the medulla oblongata.

Experimental Uræmia.—Acquisto and Pusateri (16) in dogs which died as the result of ligature of the ureters, found varicose atrophy affecting specially the pyramidal cells of the cerebral cortex, and various phases of chromatolysis, often very advanced, in the cells of the cerebral cortex and spinal cord. Sacerdotti and Ottolenghi (459), after ligature of the ureters or nephrectomy in dogs and rabbits, found changes in the nerve-cells essentially the same as those described by the preceding observers.

Experimental Anæmia.—Sarbò (485) found that one hour after ligature of the abdominal aorta the nerve-cells of the spinal cord showed disintegration of the chromatic substance of the cell-body, and "homogeneous swelling" of the nucleus. Marinesco (305) observed peripheral chromatolysis of the nerve-cells of the cord five to six hours after ligature of the abdominal aorta. The nucleus remained central. In a later paper (307) he described these changes more fully. In advanced stages he found the nucleus altered. The achromatic network of the protoplasm was disintegrated and replaced by vacuoles and even cavities. In another paper (314) he regards the morbid changes as essentially the result of œdema of the nerve-cell. Ballet and Dutil (35) observed changes very similar to those described by Marinesco. They found that commencing dissolution of the chromatophile elements could be recognised after the abdominal aorta had been compressed for only a few minutes. In advanced stages they often found the nucleus eccentric in position. Jatta (227), from the results of experiments upon rabbits, dogs and cats, has questioned the accuracy of the conclusions of previous observers. His work has been severely criticised by Lugaro, and it is doubtful if any importance is to be attached to it. Soukhanoff (481), using the method of Golgi, observed varicose atrophy of the protoplasmic prolongations of the cortical nerve-cells after ligature of both carotids.

Experimental Elevation of Temperature.—Goldscheider and Flatau (164-165-167) studied the influence of the elevation of the body-temperature in rabbits (by placing them in a thermostat) upon the nerve-cells of the spinal cord. They found that marked changes occurred as soon as the temperature of the animals was raised to 43° C. (109·5° F.). In preparations by Nissl's method the Nissl-bodies had almost completely disappeared. The cell-body was swollen, homogeneous and stained bright blue. It contained some minute granules, and presented also the appearance of a thread-network. The dendrites were pale blue and swollen, somewhat varicose and shadow-like. The nucleus was also more or less altered. Temperatures of from 41·7° to 42° C. (107-108° F.), if maintained for about three hours, produced similar but less distinct changes. The cells returned to normal in from two to three days. Lugaro (250) studied these pyrexia changes throughout the nervous system in the rabbit and dog. Summing up the results of his observations he states that the nerve-cells of animals of which the temperature has exceeded 43° present the following characters :—Profound disintegration, very marked dissolution of the chromatic part ; integrity of the achromatic part,

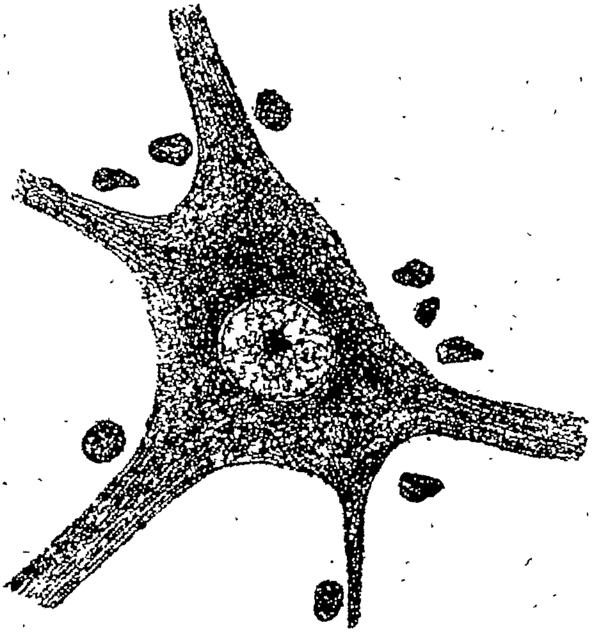

FIG. 14.

Cell of anterior horn of spinal cord of rabbit. Experimental elevation of temperature. Compare with Fig. 1. Sublimate. Thionin. (Lugaro 250.)

the reticulo-fibrillar structure of which is often rendered more evident than in the normal state; integrity of the external form and of the morphological characters of the protoplasmic and nervous prolongations; integrity of the nuclear membrane and reticulum, diminution of the colourability (with thionin) of the acidophile portion of the nucleolus, and slight modifications of form in its chromatin particles. A feature of the morbid change is that (unlike chromatolysis from most other causes) it is diffused throughout all the cells in an almost equal degree. Moxter (335), in experiments upon the effects of the local application of heat after trephining of the cord in rabbits, found that with temperatures between 40·5° and 41·5° changes occurred in the nerve-cells of the anterior horns only after twenty-two and a-half hours. Marinesco (327), who has recently also made an experimental enquiry into this subject, thinks that the alterations resulting from artificial elevation of temperature may be divided into three groups, according to the height and duration of the abnormal temperature. The first type of alteration results from the action of a maximum of heat (reaching about 47°) and a minimum of its duration (forty minutes), and consists in a dissolution of the chromatic substance only at the periphery of the cell. The second results from the action of a less degree of heat (the temperature of the animal varying during the experiment from 43° to 45°), extending over a considerably longer time, and consists essentially in those lesions described by the previous observers, except that the chromatophile elements are not always completely dissolved. The third results from the action of a temperature of about 44° for several hours, and consists of a still more severe lesion. The cell stains very deeply, has an opaque appearance, and has lost all trace of chromatophile elements. There has in this instance probably been a coagulation of the protoplasm, a lesion which is equivalent to the death of the cell. Ewing (135) records some experiments upon rabbits, which he states bear out completely the conclusions of Goldscheider and Flatau regarding the structural changes produced. The bearing of these experimental observations upon the study of nerve-cell changes in the human subject has been incidentally alluded to by several writers (162-346a) including those mentioned above, but the point is one that seems still to require careful investigation. It is obvious that in the human subject the action of the elevated temperature must in the great majority of instances be complicated by that of toxines generated in the course of the particular disease with which the pyrexia is associated. In other words, pyrexia-changes in the nerve-cells of the human subject must as a rule be combined with chromatolysis of toxic origin.

Death from cold.—D. Mirto (339), in pups killed by the action of cold, found peripheral chromatolysis and other changes in the nerve-cells throughout the nervous system. The pyramidal cells of the cerebral cortex were those most affected. Goldscheider and Flatau (167) could find no changes in the cells of the cord in rabbits which died as the result of subjection to low temperatures.

Death by electricity.—Corrado (98), in dogs killed by shocks of from 10 to 30 ampères, found very severe lesions affecting the nerve-cells. The cell-bodies showed erosions, notchings, lacerations and mutilations; the cell-outline was more or less diffuse, as if melted, or plainly irregular. Occasionally there was an appearance suggesting that part of the protoplasm had been burst out from one side of the cell by the sudden evolution of gas. The chromatic substance had undergone dissolution. Vacuolation was frequent. Changes in the nucleus were for the most part slight. With Golgi's method the protoplasmic processes showed varicose atrophy and numerous fractures, with disintegration of the fragments. Some of these processes, but especially the apical, tended to have a spiral appearance, suggesting contraction.

Among other experimental lesions of which the effects upon the nerve-cells have been studied are the following:—Cerebral abscess (Barbacci, 30), abdominal and thoracic traumatism (Parascandalo, 414), cerebral traumatism (Luzenberger, 285), slow asphyxia (Dotto, 130), intestinal auto-intoxication (Cristiani, 69, Alessi, 21).

(4) *Proliferative Capacity of the Nerve-cell.*

This question, which is one of considerable physiological and pathological importance, was for a long time a subject of dispute. It has, however, been recently most thoroughly worked out by Giuseppe Levi, thanks to whom it now rests upon a satisfactory scientific basis. Most of the previous observations upon which were founded assertions of the capacity of the nerve-cell to proliferate are necessarily of doubtful accuracy, since the histological methods employed did not permit of a distinction being clearly made between nerve-cells and neuroglia-cells. It was not until Levi had analysed the constitution of the resting nuclei by means of staining with Biondi's reagent that trustworthy criteria for such a distinction were provided.

Friedmann (138), Caporaso (77), Vitzou (514), and Tedeschi (504) maintain that they have observed the regeneration of nerve-cells; Friedmann (138), Marinesco (301), Sanarelli (477), and Tedeschi (504) believe that they have observed karyokinetic figures in nerve-cells either during repair or irritation. Marinesco (301), Sanarelli (477), Tirelli (494), and Monti and Fieschi (294) have been unable to obtain evidence that the nerve-cell is capable of regenerating.

Golgi (157) observed karyokinetic changes in the nerve-cells in experimental rabies, but thought that they represented rather a regressive process of kariolysis than a true karyokinesis. Valenza (512) was unable to observe any evidence of karyokinesis in the nerve-cells of the electric lobe of the triton after stimulation or cauterisation. In 1895 Stroebe (476) published a review of the literature of this subject.

In 1896, Levi (261), after the publication of his first paper upon the normal structure of the nucleus, briefly related some observations made with Biondi's staining upon healing aseptic wounds of the cerebral cortex of the guinea-pig. Among the abundant karyokinetic figures found especially in the healthy tissue surrounding a wound, many were in nuclei which could be proved to be those of nerve-cells from their staining reactions as well as from other evidence. A complete account of his researches upon this subject was only published last year (264). In this more recent paper he states that the object he specially set before him in his researches was to study the process of karyokinesis in nerve cells, admitting that it occurs, and to observe what deviations from the normal it presents. The methods of observation employed were those already indicated, but experiments were made upon the spinal cord as well as upon the cortex. He states the criteria which served him for the distinction of the nerve-cell nuclei from those of neuroglia and other cells. He found that the process of karyokinesis in the nerve-cells has, in its early phases, certain special features dependent upon the peculiar structure of the nucleus. It is doubtful if it would serve any purpose to endeavour to describe this process here. Anyone who desires to understand the matter must necessarily consult the original paper, and follow the description of the process with the aid of the beautiful coloured plates by which it is illustrated. Levi has only been able to observe karyokinesis in the medium-sized and small pyramidal cells of the cortex of the guinea pig. He could not find it in very highly differentiated nerve-cells, such as the large cells of the cord and brain. Although he has never observed complete division of a nerve-cell, he is inclined, from the advanced stages of karyokinesis that he has observed, to think that it can occur. It is probable, however, that such multiplication of nerve-cells is simply a reaction to the stimulus that has affected them and that it does not lead to a stable regeneration. In favour of this view is the fact noted by several observers that the proliferation of the nerve-cells is most active from the second to the fifth day, afterwards diminishing gradually and ceasing about the twentieth day. He thinks that very highly differentiated nerve-cells, when affected by a stimulus, undergo degeneration instead of attempting to multiply. Their reproductive capacity has become lost in favour of that of fulfilling their special function. The index of this loss of reproductive capacity is probably the paucity of nuclein, which, as has been seen, diminishes with the higher differentiation of the cells.

(5) *Post-mortem Changes in Nerve-Cells.*

This subject, the importance of a thorough knowledge of which to the neuro-pathologist must be obvious, has recently been studied experimentally by several observers. Tirelli (497) in his lengthy work upon the chronology of the death of the elements of the nervous system, which is chiefly of medico-legal interest, states that nine hours after death there can be observed a diffusion of the chromatic substance into the achromatic part of the protoplasm. The cell-body then assumes a finely granular aspect throughout. According to Colucci (89) the chief alterations are a diffuse granular disintegration of all the cell-elements excepting the nucleolus, pale and turbid staining with methylene blue, loss of affinity for this stain in tracts of the prolongations, rupture of the protoplasm in various directions in many cells, &c. Neppi (377) studied the cadaveric alterations in the cells of the anterior horn of the spinal cord of the dog, using sublimate fixation and thionin staining. He could not find distinct changes until forty-eight hours after death. They consisted chiefly in dissolution of the chromophile substance (the particles of which first showed badly defined outlines and then diminished affinity for the stain) and diffuse colouration of the nucleus. The nucleolus was only affected at a very late period. The cells tended to shrink and not to swell as in chromatolysis. Barbacci and Campacci (29) have made a very elaborate series of observations upon rabbits killed by bleeding and afterwards kept at a uniform temperature of 22° C. After various periods they examined different portions of the central nervous organs by the methods of Nissl (sublimate-thionin modification), Cox and Marchi. Their description of the changes observed is full of minute details of which it is impossible to give an accurate epitome. They state that the first alteration as a rule consists in the progressive paling of the chromatic particles. These next generally break up into fine granules which become smaller and smaller, giving the protoplasm a characteristic powdery look; sometimes, on the other hand, there is a fusion of the particles into irregular masses. Later the protoplasm assumes a pale, finely granular appearance and tends to lose its regular outline. The nucleus undergoes a dropsical change which leads to its rupture and shrinkage. It then appears as an irregular homogeneous mass which stains deeply. The nucleolus only at a very late stage becomes pale, irregular in form and displaced. In preparations by Cox's method there is detachment of the gemmulæ, erosion and breaking across of the protoplasmic processes and cell-bodies. Later the whole element assumes a very characteristic powdery aspect. Giulio Levi (269) has also carried out a vary careful investigation into this subject upon rabbits, using the sublimate-thionin method. His results differ from those of the preceding observers, chiefly in regard to one point. He describes an initial hyperchromic phase, or a condition of abnormally deep staining of the chromatic elements which precedes that of pallor and fragmentation. França (150) has obtained in guinea-pigs results which are essentially in agreement with those of previous observers. Tirelli (498) has recently made a comparative study of the appearances of cadaveric and pathological changes in the brain of the rabbit with the aid of the rapid silver method. His results are not at all in accord with those obtained by Barbacci and Campacci with Cox's method, to which, however, he does not refer. He finds that even somewhat advanced putrefaction does not deprive the nerve-cells of their characteristic aspect in silver preparations. An excellent account of these cadaveric changes has been given by Ewing, both in his preliminary communication (134) and in his comprehensive monograph upon ganglion cells (135). In his first paper he notes especially deep diffuse staining of the nucleus at an early stage, shrinkage of it and of the nucleolus in advanced stages; granular subdivision of the chromophilic bodies and reticulum, without actual loss of chromatic substance, which gives to the cell-body a characteristic uniformly granular appearance. In his more recent work, he deals with the subject still more fully and describes some experimental observations upon the rabbit. In addition to the above changes he mentions the occurrence of vacuoles in the protoplasm which he believes to be one of the most constant of *post-mortem* products. The writer and Orr (457) have described and figured these *post-mortem* changes as observed in the cortical nerve-cells of the human subject in methyl violet preparations, and have pointed out how they are to be distinguished from genuine chromatolysis.

III. TYPES OF MORBID CHANGE AFFECTING THE NERVE-CELL.

(1) *Chromatolysis.*

The term "chromatolysis," introduced by Marinesco (305), implies, strictly speaking, merely disintegration of the chromatic particles of the protoplasm—breaking up of the aggregations of granules that form the Nissl-bodies and gradual disappearance of the individual granules, accompanied in transition stages by their diminished affinity for basic dyes. But it has been frequently used in a wider and more general sense, namely, to indicate the whole series of changes in the constituent elements of the cell, of which dissolution of the chromatic particles is merely the first that is recognisable. The term has therefore in the meantime its narrower and its wider senses. I use it here only in its narrower sense.

The various causes of chromatolysis, and the different appearances that it presents, have probably already been sufficiently illustrated in the preceding section. It remains for me here merely to briefly notice certain general facts and opinions regarding the morbid process, and to refer to its occurrence in the human subject.

Chromatolysis may be peripheral, perinuclear, or diffuse; partial or complete. It may occur as an acute or as a chronic change. Comparatively little, however, is known about its chronic forms, owing chiefly to the greater difficulties which they present in the way of experimental investigation. A typical example of chronic chromatolysis is that which occurs in senile involution of the nerve-cell.

The mechanism and significance of chromatolysis have given rise to much discussion. The following papers contain special reference to this subject:—Lugaro (242-250), Marinesco (312-314-327), van Gehuchten (170-173), Goldscheider and Flatau (164-165-167), Ballet and Dutil (35). In 1896 Lugaro (242) stated that the exact mechanism of chromatolysis was still uncertain and obscure. The matter can scarcely be said to stand otherwise to-day. Regarding the significance of chromatolysis much has recently been written. It is to be remembered that the function of the Nissl-bodies is still in dispute, and it is therefore only to be expected that the significance of their disintegration should also be a matter of difference of opinion. In the paper just referred to Lugaro maintained that alterations of the chromatic part do not represent more than a reaction of the cell to a disturbing force and are reparable; while on the other hand alterations of the achromatic part are to be regarded as degenerative and irreparable. This view, which had been foreshadowed by Marinesco (305), has since been very generally accepted as in accordance with the facts. Goldscheider and Flatau, from their observations upon the occurrence of chromatolysis in experimental pyrexia and in malonnitril poisoning, were led to maintain that the Nissl-bodies have no great importance either for the vitality or the functional activity of the cell, and that chromatolysis has little significance as a pathological change. An animal with its motor cells thus markedly altered was still able to perform all kinetic functions. Lugaro (250) states that he cannot accept these opinions in their entirety. According to his own observations, although the motor functions may be preserved apparently intact in experimental pyrexia, with the progress of the alterations there is a motor weakening. The chromatic part fulfils its functions through its chemical, not through its morphological, structure. Its quantitative and structural integrity is not essential for motor function, yet its progressive dissolution causes progressive weakening of that function. The morphological conditions necessary to function consist in the structure of the achromatic part and in the connections between the various nervous elements, determined by the disposition of the cellular arborisations. While these morphological conditions are preserved, the possibility of functional activity is also preserved, but its intensity depends upon the quantity of the chromatic substance existing in the cell. This substance has, without doubt, an important and indispensable part in the functional metabolism of the element. Marinesco (327) has supported Lugaro's opinion in this matter, and has expressed himself even more emphatically with regard to the importance of the chromatophile elements for the vitality and functional activity of the cell. His own experimental observations have led him to conclude, contrary to the opinion of Goldscheider and Flatau, that cells that have reached a state of absolute achromatosis cannot recover.

Chromatolysis has been observed in the human subject in a very large number of different morbid conditions. Indeed it is now known that it occurs in some degree in a proportion of the nerve-cells of almost every individual dying a natural death. Even in non-nervous diseases it is very commonly an extensive and well-marked morbid change in the cells of the cerebral cortex, spinal cord, &c. In such cases it is to be attributed to the action of toxic substances generated in the course of the particular disease, to pyrexia, terminal auto-intoxication, or to local vascular lesions (286). At the same time abundant evidence has now been accumulated of the special incidence of chromatolysis in various forms of nervous disease. A list of recent papers dealing with the morbid changes in the nerve-cells in various diseases in the human subject is appended to this section. In practically all of these papers that describe the results of examinations with the method of Nissl, as most of them do, there will be found recorded the occurrence of disintegration of the chromatic elements of the protoplasm.

(2) *Achromatolysis or Plasmolysis.*

These terms have been applied by Marinesco (314) to one of three different morbid changes which have been recognised by him and others to occur in the constituent elements of the achromatic part of the cytoplasm, either simultaneously with or consecutive to chromatolysis in the narrower sense. He describes it as consisting of a molecular disintegration of the achromatic substance. It is to be observed that he does not restrict the terms to disintegration of the formed or fibrillar portion of this substance. Loss of the primitive fibrils and their replacement by powdery granules is, however, practically the only visible alteration in achromatolysis. It was Lugaro (242) who first described this alteration, and he has since given several minute descriptions of it as observed in various experimental lesions, more especially in hæmatoxylin preparations.

(3) *Coagulation of the Achromatic Substance.*

This is the second lesion of this part of the cytoplasm distinguished by Marinesco (314). He describes it as consisting in the coagulation, and probably the chemical transformation, of the achromatic substance into a colourless mass of vitreous aspect. It is most typically seen in the cells of the spinal cord after ligature of the abdominal aorta.

(4) *Intense Colourability of the Achromatic Substance.*

This is the third morbid change distinguished by Marinesco (314) in this substance. It is displayed especially in preparations by Nissl's method and its modifications, and has been noted by several observers, more especially in poisoning by arsenic and antimony, and in Landry's paralysis.

(5) *Varicose Atrophy.*

This term has been applied to certain morbid appearances sometimes to be observed in the nerve-cells in preparations by Golgi's method and its modifications. It consists in the presence of irregular swellings or varicosities in the course of the protoplasmic prolongations, partial or complete disappearance of these prolongations and shrinkage and deformity of the cell-bodies. It is certain that such abnormal appearances in Golgi preparations may be the result of genuine pathological changes in the form of the cell; but it is equally certain that many of its slighter manifestations, more especially varicosities, may be, and in many published descriptions have been, of a purely artificial character. It is to be borne in mind that the presence of varicosities on the protoplasmic prolongations is normal in the fœtus. Loss of the gemmulæ has sometimes been referred to as a distinct morbid alteration, but it can scarcely be separated from varicose atrophy. The subject is one of considerable importance and therefore I give a somewhat detailed account of its literature.

In 1893 Colella (91) described the occurrence of varicose changes in the nerve-cells in general paralysis. In 1894 Golgi (157) described similar alterations in experimental rabies. They resembled those that he had described in chorea in 1874. Ceni (71) found them in secondary degeneration of the cord, Andriezen (12) in alcoholic insanity. Klippel and Azoulay (4) in general paralysis and melancholia. The last-named authors stated that the alteration began as an abrasion of the gemmulæ, or as an agglutination of them, and that it spread gradually from the periphery of the protoplasmic prolongations towards the cell-body.

In 1895 Berkley (22) described changes similar to those just mentioned in chronic alcoholic poisoning in rabbits. In another paper (24) he recorded the observation of the loss of a large number of the gemmulæ in secondary dementia, Ceni (72) described varicose atrophy in the cells of cerebellum after lesions of the cord, Tirelli (495) in the cerebrum of general paralytics, and of epileptics dying in *status epilepticus*, Pernice and Scagliosi (405) in diphtheritic infection, Monti (290) in experimental embolism, and (291) in inanition.

In 1896 Demoor (107) described the production of varicosities upon the protoplasmic processes by the action of morphia, chloral and chloroform, as well as by that of prolonged electrical stimulation, and their disappearance on the return of the elements to normal conditions. Berkley (26) gave a further account of the varicose changes in the cortical nerve-cells of rabbits subjected to chronic alcoholic poisoning, describing especially a distinct diminution in the size of the cells, a shrinkage of the vast majority of them, swellings of the dendritic processes with disappearance of the gemmulæ, and roughening of the stronger processes and to a less extent of the cell-bodies. At the same time, he drew attention to certain " normal inequalities or varicosities in the construction of the dendrons." In another paper (27) he described the changes produced by experimental acute alcoholic poisoning as revealed by his modification of Golgi's silver method, mentioning specially irregular tumefaction of the protoplasmic processes, and considerable loss of the lateral buds, with or without such tumefaction. Dotto (128) described varicose atrophy in chronic poisoning by perchloride of mercury, and (129) by quinine and ergotinine; Ceni (73) in the cells of the cerebral cortex after section of the spinal cord in dogs, and (74) in diphtheritic poisoning (chiefly experimental). Lugaro (242) drew attention to the difficulties that surround the employment of Golgi's method in pathology. He stated that alterations simulating varicose atrophy were readily produced by defects of fixation, such as commonly resulted from the use of bichromate of potassium either alone or with osmic acid. He recommended the use of Cox's solution, even with which, however, the pieces should not exceed 1 cm. in thickness. He attributed to such imperfect fixation the results obtained by Demoor, whose experiments he had repeated with totally negative results. All these reservations, however, did not prevent the acceptance of varicose atrophy as a real anatomical alteration, as it had been observed in experimental material examined with the most rigorous technique. Its exact value could not yet be established. It could be excluded, however, that it expressed a simple disturbance of the nutrition of the element, or an initial alteration. It probably represented a final destructive process which revealed itself first in the most delicate parts. Ramon y Cajal (428) also drew attention to the production of these varicose changes by defective methods of examination. Acquisto and Pusateri (16) observed varicose atrophy of many of the cells of the cerebral cortex in acute experimental uræmia.

In 1897 Sacerdotti and Ottolenghi (459) confirmed the immediately preceding observation. Dotto and Pusateri (131), from a study of the cortex in a case of cerebral hæmorrhage, supported the opinion of Lugaro that varicose atrophy represents not an early, but a late phase of alteration in the nerve-cells. Lugaro (245), in his investigations of the changes in poisoning by arsenic and lead, obtained further important evidence in support of

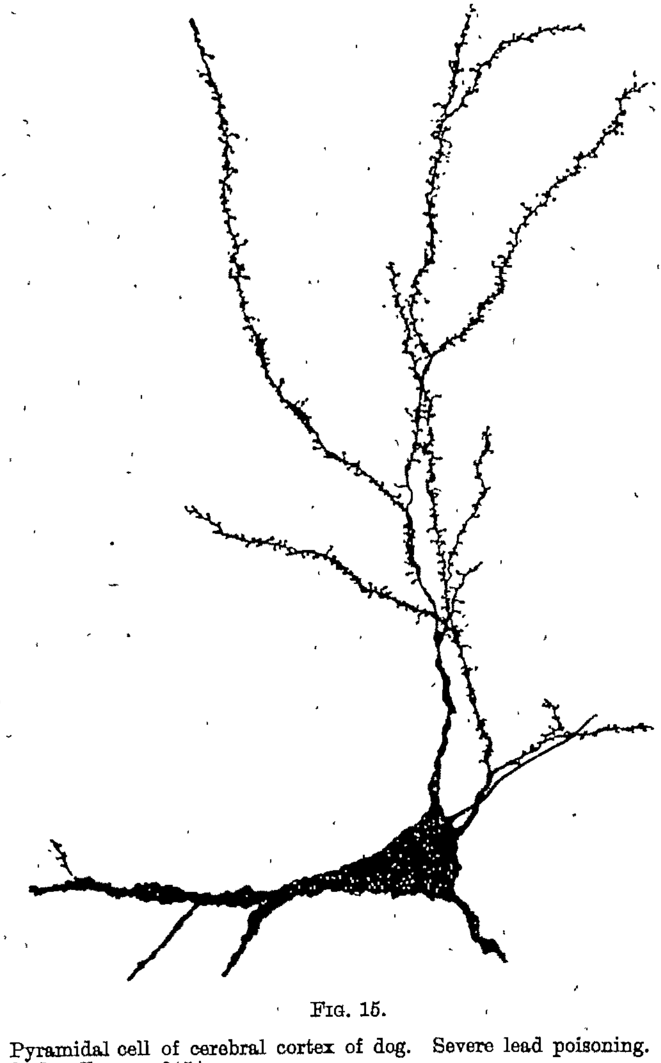

FIG. 15.

Pyramidal cell of cerebral cortex of dog. Severe lead poisoning. Cox's method. (Lugaro 245.)

this conclusion. He found that even when there are distinct cytological alterations the external form of the nerve-cell, as revealed by Cox's method, may appear quite intact. When alterations did appear they affected specially the cell-body and large protoplasmic trunks, and notwithstanding their presence the fine branches and the gemmulæ might be preserved. He expressed himself as more than ever doubtful of the pathological value of swellings in the form of a rosary, preceded by loss of the spines and invading the protoplasmic prolongations progressively. He had been able to prove that such varicosities could be produced in enormous numbers by the employment of fixatives that are not very energetic and of too thick pieces of tissue. Further, he believed that mechanical maltreatment of the pieces and their subjection to the action of the air could produce similar modifications. In support of the latter point, he referred to the fact that Ramon y Cajal (428-429) had been able to demonstrate that the numerous varicosities which appear in preparations by the Ehrlich-Dogiel method in all prolongations of the nerve-cells are due to the altering action of the air. Lugaro adds that sometimes in normal preparations treated with all possible precautions, there are to be observed some prolongations with the characters of the so-called varicose atrophy, which are certainly due to some cause of alteration that has escaped notice. Lugaro and Chiozzi (258), in their observations upon the changes resulting from inanition, found that varicosity occurred only at a very late stage of the cellular alteration, and that it was not preceded by disappearance of the spinous appendages.

In 1898 Monti (293) described, in the nerve-cells of animals subjected to inanition, varicose atrophy proceeding regularly from the extremity of the dendrites towards the cell-body. He maintained that the dendrites were the first to undergo alteration in inanition, and that there exists a perfect correspondence between this alteration and chromatolysis, both of which were to be observed in disturbance of the nutrition of the nerve-cell. This paper elicited from Lugaro (249) a very vigorous criticism, which, however, was not directed solely against the views just mentioned. He maintained that the appearances described were nothing more than artificial products depending upon errors of technique. In his observations upon experimental pyrexia (250), he found that the extreme chromatolysis thereby produced is not accompanied by any alterations of the protoplasmic prolongations in Cox preparations. Batty Tuke (503) has recently accepted as demonstrated the loss of the gemmulæ of the dendrons under the action of disease. It must be replied that, however probable such an occurrence is, the evidence that has yet been adduced in support of it is not decisive. Peters (413a) concludes that the gemmulæ are diminished in correspondence with the degree of intellectual decadence in the insane. Wright (523) describes varicose changes in the cortical nerve-cells in accidental and experimental poisoning by potassium bromide. Soukhanoff (481) describes gross changes in the form of the protoplasmic prolongations in experimental cerebral anæmia, and Corrado (98) in death by electricity. The writer and Orr (457), following essentially the technique advocated by Lugaro, have observed in the human brain in various pathological conditions occasional varicose changes corresponding to those recognised as genuine by that authority. Demoor (107-108) Stefanowska (474), Querton (417), Manouelian (300) and Odier (389), have described varicosities of the protoplasmic processes, with or without disappearance of the gemmulæ, as evidence of contraction in various functional modifications of the nerve-cells. On the other hand, Azoulay (3) has been unable to obtain such evidence, and Lugaro (252), by injection of the vessels of the living brain with Cox's fluid, has also obtained results contrary to the conclusions of these observers.

(6) *Varicose Hypertrophy of the Axis-cylinder Process.*

This is another morbid appearance that may not infrequently be observed in preparations by Golgi's method. It consists, as the name that has been given to it implies, in globular, fusiform or irregular swelling in the course of the axis-cylinder process. It was first recognised by Golgi in

1874 in chorea, and afterwards in rabies (157). Colella (91) believes that it is sometimes a primary change in general paralysis. In 1896 Lugaro (242) expressed the opinion that it was improbable that the condition could be separated from lesions of the cell-body, but at the same time seemed to doubt if it was a genuine pathological alteration at all. Numerous incidental references to these varicosities are also made in other papers, but the subject seems to be one that still requires to be placed upon a sound scientific basis. The writer and Orr (457) have described and figured a more gross change in the axis-cylinder processes in the human brain in various pathological conditions, and have expressed the opinion (which they believe is in agreement with that of Lugaro) that simple swellings in the form of a rosary are not necessarily pathological alterations at all. Illustrations of these varicose changes will also be found in the text-book of Clouston (100).

(7) *Pigmentary or Yellow-globular Degeneration.*

Neurologists in this country have been made familiar with the subject of pigmentary degeneration of nerve-cells more especially through the writings of Bevan Lewis. On the Continent comparatively little importance is attached to this transformation, about the only recent writer who deals with it at any length being apparently Colucci, who, however, objects to the term "pigmentary" and adopts that of "yellow-globular degeneration." The nerve-cell pigment in normal conditions has already been considered in another section (I. 5), which should here be referred to by the reader.

Pilcz (392), in his important work on nerve-cell pigment, states that the pale yellow variety continues to increase with age in the human subject. This statement is confirmed by many other observers. Hutchison (209) does not accept Bevan Lewis's statement that the accumulation of pigment is "invariably a witness to byegone functional hyper-activity." He has found such accumulation to be the rule rather than the exception in the human brain. He believes that pigment is specially increased in renal disease, and that it is not more abundant in the insane than in the mentally sound. The views of Colucci (89) upon this subject do not appear to be so well known in this country as they deserve to be. He objects to the term "pigmentary degeneration" on the ground that it is not proved that the globules are true pigment granules, and that it is probable that they are really a product of metabolism in the cell. He thinks that all the elements at the spot are probably involved in the transformation, as every trace of the original structure disappears. He describes the appearances that the globules present in normal and pathological conditions. The criterion of degeneration is especially their appearance in portions of the cell that are not normally provided with them, as at the base of the protoplasmic prolongations and in the peripheral zone. Occasionally the nucleus becomes affected. The yellow globules undergo various transformations, the most common being fatty and pigmentary degeneration. In the latter they may become quite black. He thinks that yellow-globular degeneration is most marked in slow dementias such as epileptic dementia and general paralysis. Lugaro (245), in experimental lead poisoning in the dog, observed in the cells of the spinal ganglia and cerebral cortex the occurrence of yellow pigment granules, which are normally wanting in these elements in this animal. Adolf Meyer (344) has described the various manifestations of pigmentary degeneration in the giant cells of the para-central lobule. Cristiani (68), Turner (493) and Lord (289a) have published papers in which pigmentary changes are described as observed in the brains of the insane. Bevan Lewis (272), in the second edition of his important text-book, has recently given a very full account of his views regarding "pigmentary or fuscous degeneration." He holds to his opinion that excessive pigmentation is a witness to byegone functional hyper-activity, and does not notice the criticism of Hutchison. He maintains that the fuscous state is not truly a degeneration of the cell-protoplasm, although it may be accompanied by it, or be its immediate cause. He gives a minute description of the various phases of excessive pigmentation, which he divides into three stages or periods, namely, those of over-activity, diminished activity and absorption. Epileptic insanity and general paralysis are the forms of mental disease in which he has found the nerve-cells most prone to this morbid change.

It remains to be added that pigmentary degeneration is obviously identical with one or more of the slowly progressive or chronic forms of chromatolysis, and that the fact of real importance in the morbid alteration is not the accumulation of an abnormal quantity of yellow granules, but the associated destruction of the spongioplasm and trophoplasm. The present state of our knowledge of the subject does not, however, permit of a definite conclusion as to which of these changes is the primary one.

(8) *Vacuolation.*

Vacuolation of nerve-cells has recently been the subject of special papers by Campbell (84) and Skae (458), and it has also been considered somewhat fully by Colucci (89), van Gehuchten and Buck (178), Bevan Lewis (272), and Ewing (135). Its occurrence has further been incidentally described by Daddi (109) in passive congestion, by Piccinino (399) in a case of Landry's paralysis, Ceni (75) in experimental acute septic meningitis, by Corrado (98) and Fish (147) in death by electricity, by Marinesco (320) in paraplegia, by Berger (53), and Anglade (15) in general paralysis, by Soukhanoff (482) in arsenic poisoning, by Köster (235) in carbon bi-sulphide poisoning, and by Sarbò (485) and Marinesco (307) after ligature of the abdominal aorta, and by many others.

It would serve little purpose to give an outline of the views expressed regarding vacuolation in each of these publications, for it is the plain fact that no satisfactory investigation upon this morbid change has yet been recorded. The truth of this contention is fully recognised by van Gehuchten and Buck, who, after reviewing the literature of vacuolation and stating practically all that is definitely known about it, conclude that further research is required on the subject before precise statements can be made regarding it.

The important facts that have been established may be summed up in a few words. Vacuolation may affect either the nucleus or the protoplasm, or both; it consists in the formation in the cell-substance of one or more, small or large, non-colourable globules which are probably most commonly of a fluid character, although the observations of Corrado demonstrate the possibility of their sometimes being vacuoles in the stricter sense of the term; when fluid in character, they may almost certainly be composed of essentially different substances in different instances. They are undoubtedly composed of fatty matter in certain instances, but the assertion that they are, as a rule, of this nature has not been satisfactorily proved, and is probably erroneous. The various causes that determine their formation, the processes of their development, the associated changes in the chromatic and achromatic substances of the protoplasm and in the various constituents of the nucleus, and their pathological significance, have yet to be determined.

(9) *Fatty Degeneration.*

The possibility of the occurrence of fatty degeneration in nerve-cells as in other cell-elements seems now to be satisfactorily demonstrated, although at one time it was denied. Elkins and Middlemass (137) observed it in an extreme form, affecting both protoplasm and nucleus, in a case of phosphorus poisoning. It seems certain that vacuolation in some of its manifestations depends upon the formation of fatty globules; it has been noted also that in pigmentary degeneration the yellow globules are capable of undergoing a fatty metamorphosis. Lastly, Lugaro (245) and others have observed fat granules in nerve-cells affected by chromatolysis.

(10) *Displacement of the Nucleus.*

In advanced stages of chromatolysis (in the wider sense) the nucleus tends to become displaced or dislocated to the periphery of the protoplasm. It may come to project beyond the surface of the cell, and occasionally, according to some authorities, may even be completely extruded. Lugaro has maintained that the true significance of this displacement of the nucleus is that the achromatic reticulum, which normally holds the nucleus in its generally central position, has become destroyed.

(11) *Homogeneous Degeneration of the Nucleus.*

In 1895, Sarbò (485) described in the cells of the spinal cord, affected by chromatolysis after ligature of the abdominal aorta, a peculiar change affecting the nucleus and characterised by a homogeneous aspect, deep staining with methylene blue, and atrophy. He designated it *acute Homogenesirung mit atrophie.* This expression cannot be rendered literally in English, but probably it is sufficiently represented by "homogeneous degeneration." Many writers in describing similar appearances of the nucleus in various morbid conditions identify them with this change described by Sarbò. Among these writers may be mentioned Colucci (90), Donaggio (103), and Lugaro (246), the last of whom briefly indicates the parts that the acidophile and basophile constituents of the nucleus appear to play in the morbid alteration. The pathology of the nucleus of the nerve-cell has still to be written, and until this is done it is impossible to say whether or not we are justified in regarding "homogeneous degeneration" as a special morbid change.

(12) *Invasion by Bacteria.*

While it is certain that bacteria exert their morbid influence upon nerve-cells practically only by means of the easily diffusible toxines that they generate, the observation of the occurrence of these organisms within the cell-body is one of considerable interest and importance. Such observations have recently been made by Nissl (371), Piccinino (399), and Babes (43). Piccinino found a diplococcus in the acutely degenerated nerve-cells of the spinal cord in a case of Landry's paralysis, while Babes observed the specific organisms in nerve-cells in plague, leprosy and other infective diseases.

(13) *Loss of Nerve-Cells.*

Death and total disappearance is the fate of a certain percentage of nerve-cells affected by acute primary lesions. Whether or not the same result occurs in secondary lesions is a matter of dispute. Chronic forms of chromatolysis, such as that which occurs in senility, must also, it is evident, result in the loss of large numbers of nerve-cells. The question of the manner in which the dead nerve-cells are removed is one that has given rise to some dispute. Marinesco (314) thinks that proliferated neuroglia cells conjointly with leucocytes act as destroyers of degenerated nerve-cells. Bevan Lewis (272) believes that certain large cell-elements of the neuroglia are the all-important elements in this connection. Turner (491) describes leucocytes as attacking, destroying and removing nerve-cells in the cerebrum in senile insanity and other morbid conditions. Pugnat (397) has described the invasion and removal of degenerating nerve-cells by leucocytes in senility, an occurrence which he attributes to the diminished resisting power of the nervous elements. Nissl (368), in his paper upon general paralysis, maintains that the nuclei to be observed upon the degenerating nerve-cells are only those of neuroglia cells, and that leucocytes are never to be observed in this position. Lugaro (254) supports Nissl's view from his own observations. He states that he has searched in vain for leucocytes in the cortex of paralytics and in that of the rabbit in meningo-encephalitis. Neuroglia-cells are to be observed grouped about the pyramidal nerve-cells in the healthy state. Their nuclei are sometimes so planted on the nerve-cell as to simulate a lymphoid element in the act of penetrating it. The writer and Orr (457) have stated that in many cases of secondary dementia it can be satisfactorily demonstrated that about 50 per cent. of the cortical nerve-cells have entirely disappeared. The loss of nerve-cells which occurs in the spinal cord and posterior root ganglia after amputations has recently been described by Campbell (85).

(14) *Developmental Arrest.*

As loss of nerve-cells is the most important fact in the pathological anatomy of secondary dementia, so arrest of development of nerve-cells at some stage in their growth is the most important fact in that of certain forms of idiocy and imbecility. Hammarberg (200) made a most complete examination of nine brains from such cases, the results of which furnish most convincing evidence upon this point. A good account of his work is given by Ireland (218). Bevan Lewis (272) has found developmental arrest of nerve-cells only in epileptic idiocy and has failed to find it in simple forms of congenital defect and deaf mutism. Köppen (230) observed arrest of development of nerve-cells in one case of idiocy and paucity of cells in another. Ireland (218) refers to a case observed by the writer in which there was a zone of developmental arrest running through the layer of large pyramidal cells throughout both hemispheres.

(15) *Other Types of Change described.*

The above list by no means exhausts all the forms of morbid change that have been described in the nerve-cell. "Granular disintegration or degeneration" is still described by Bevan Lewis (272) as a separate pathological entity. It is a change revealed by his fresh method, and the description that he gives of it leaves little doubt in the writer's mind that it is to be identified with various manifestations of chromatolysis, including its acute forms and chronic senile form. Colucci (89) describes granular degeneration but recognises its identity with chromatolysis. It is to be mentioned also that Nissl (367-368) in 1896 described four disease-forms of the cortical nerve-cell in general paralysis; and more recently (374) he has drawn special attention to an acute alteration affecting the whole nerve-cell,—body and processes,—and all the cells of the cortex simultaneously.

Index of papers in Bibliography containing descriptions of nerve-cell changes in various morbid conditions in the human subject.

Landry's paralysis, 314, 315, 298, 388, 56, 399, 455, 184.
Locomotor ataxia, 311, 44, 170, 467, 468, 469, 464, 221, 270, 244, 342, 232, 233, 181, 402, 453, 347, 311, 383, 297, 385.
Bulbar paralysis, 314, 315, 517.
Infantile paralysis, 333.
Peripheral neuritis, 143, 144, 145, 303, 305, 307a, 314, 321, 473, 480, 37, 242, 123, 31, 32, 163, 287.

Epidemic cerebro-spinal meningitis, 61.
Paraplegia, 174, 521, 320.
Tetanus, 183, 454, 217, 403, 114.
Diphtheria, 43, 405, 74.
Rabies, 478, 86.
Acute chorea, 187.
Pellagra, 440, 441, 438.
Paralysis agitans, 86, 36, 181.
General paralysis, 367, 368, 53, 34, 15, 4, 495, 31, 32, 19, 20, 195, 57, 193, 416, 89, 272, 68, 91, 92, 222.
Acute alcoholism, 207, 507.
Acute insanities, 207, 70, 5, 6, 457, 100, 502, 19, 272.
Epilepsy, 76, 329, 220, 442, 495, 415, 89, 272, 68.
Mental confusion, 33, 6.
Secondary dementia, 296, 24, 457, 413a, 272, 6.
Idiocy and imbecility, 200, 13, 230, 218, 100, 272.
Pernicious anæmia, 58, 185.
Fevers, 327, 162, 346a, 124, 317.
Various non-nervous diseases, 134, 209, 457, 508, 86, 135, 286, 60, 208.

IV.—Addendum upon Physiological and Pathological Deductions.

Although the purpose of this digest is to give an account of observations relating only to the morphology of the nerve-cell, it has seemed to me that the importance of a number of the structural details that are described cannot be correctly appreciated except in the light of certain closely related physiological questions that are now the subject of controversy. For this reason I add a brief account of recent views upon some of these questions.

The present position of the Theory of the Neuron.

As is well known, the neuron theory has always been opposed by Golgi. Recently he has firmly maintained his position in the matter, and has promised a further demonstration of the existence of his diffuse network (159-160). The numerous alleged observations of direct connections between nerve-cells that have lately been made have also a certain weight of argument against the doctrine of the neuron, but the really serious attack that has been made upon this doctrine, which was generally thought to be so firmly established, is that for which Apáthy is primarily responsible. His very remarkable conclusions regarding the structure of the nervous system of certain invertebrates, of which an account has already been given (Section I., 9), are in certain respects supported by the observations of Bethe, and they have been accepted by Nissl (374-375). There are now many who have been led to believe through the writings of these authorities that the neuron theory has been proved to be false. It is becoming evident, however, that this is not the view that is going to be taken by those authorities whose judgment in such a matter is most valued by the great majority of neurologists. Among these authorities Lugaro (256), and Lenhossék (283) have already spoken in a very decided manner. Lugaro's contribution to the controversy takes the form of a long *recensione* of the paper in which Nissl (374) announced his acceptance of Apáthy's teaching and declared his belief that the neuron theory is no longer tenable. It would be impossible to give an accurate outline of Lugaro's closely reasoned and most valuable critique. It should be read by all who desire to understand the true factors in this controversy, and more especially by those who have hastily concluded with Nissl that the neuron theory has received its death blow. Lugaro maintains that the observations of Apáthy and Bethe do not warrant the general conclusion that nerve-cells are connected with each other by means of their primitive fibrils, and considers that Nissl has been too precipitate in adopting this view. Even admitting Apáthy's demonstration of a continuous network formed by these fibrils outside the nerve-cell in certain invertebrates, such an arrangement has not yet been proved to exist in vertebrate animals, while there is the strongest histological evidence that it does not. Lenhossék (283), whose article is a critical review of a paper by Bethe (50), can find in the discoveries of this observer and also in those of Apáthy nothing that contradicts the neuron theory. He thinks that Apáthy's conception of the central neuropil as a true diffuse elementary network has not been conclusively demonstrated. In any case it is but the view of a single observer. It is entirely erroneous to cite Bethe's observations in support of Apáthy's views, for Bethe has himself declared that he has been unable to convince himself of the existence of a true network in *carcinus mænas.* With regard to Bethe's now famous experiment upon this animal, Lenhossék denies that in it the conditions have been fulfilled that would give to its results any surprising character.

Among other recent papers dealing with the theory of the neuron the following may be mentioned:—Tanzi (499), Schäfer (471), Golgi (158), Marinesco (302), Renaut (450-451), van Gehuchten (168), Soury (483), Klippel (232), Barker (62), Dercum (127), and Goldscheider (161).

Function of the Protoplasmic Prolongations.—There are two opposing views at present held with regard to the function of the protoplasmic prolongations. Firstly, there is that of Golgi, according to which they have a merely nutritive function without subserving that of nervous conduction; and, secondly, there is that supported by the large majority of other authorities according to which this portion of the the nueron is essentially related to nervous conduction. Of recent papers dealing with this controversy probably the most interesting are those of Golgi (159) and Lugaro (251). The former found in his pericellular reticulum a new and important argument in support of his opinion, while the latter criticised Golgi's paper and defended the more generally accepted view. Several observers, on the ground of the observation of varicosity of the protoplasmic processes advancing centripetally in certain morbid conditions, have maintained that these processes must have a nutritive function. The fallacious character of such evidence has been repeatedly maintained by Lugaro (see especially No. 249).

The Law of Dynamic Polarisation.—The enunciation of this law has very commonly been attributed to Ramon y Cajal (419), but van Gehuchten (168) has maintained, evidently upon good grounds, that it was really he who was the first to advance it. According to this law or theory (which has been very widely accepted), as originally stated, the nervous current is cellulipetal in the protoplasmic processes and cellulifugal in the axis-cylinder process; in other words, the dendrites are the organs of reception of the nervous impulse, the axon is the organ of their distribution and application. In order to obviate certain objections to this theory, and to permit especially of its being applied to the case of the cells of the spinal ganglia, both Ramon y Cajal (432) and van Gehuchten (168) have proposed to slightly alter its formula. The former thinks that there may be a direct passage of the nervous current from a dendrite to an axon arising from it, and that we should therefore speak of the nerve-current as *axipetal* (instead of cellulipetal) in the dendrites, and *dendrifugal* (instead of cellulifugal) in the axis-cylinder process. Van Gehuchten regards the large protoplasmic processes and the cell-body as forming together the true cellular body, and believes that the conduction is here indifferent, occurring in any direction. Tanzi (500) thinks that Cajal's new theory is unnecessary, and is inclined to admit the correctness of van Gehuchten's view, but insists more upon the fact of the fibrillar structure of the prolongations, and therefore of the possibility of conduction in them in both directions. He points out that Cajal's imagined correction of the law of dynamic polarisation does not remove its essential defect, which consists in the necessity of considering as gigantic dendrites the peripheral sensory fibres coming off from the cells of the spinal ganglia, although they are medullated and do not differ in any respect from the nervous prolongations. Lugaro (247) considers that neither of the new interpretations are necessary, since the fibrillar structure of the prolongations admits of a double conduction and of the separate existence of dendrite and axon in a common trunk, such as that given off by the cells of the spinal ganglia.

Function of the Chromatic and Achromatic Parts of the Cytoplasm. — There are at present two principal views regarding the function of the chromatic substance of the cytoplasm. According to the first, which is supported by van Gehuchten, Nissl, Lugaro, Lenhossék, Cajal, and many others, it is "a material of reserve destined to serve for the nutrition of the nervous elements" (168). According to the second, which has been advanced by Marinesco (305), "it serves to augment the difference of potential of the centrifugal nerve wave." Marinesco has very fully explained his views upon this point in his *Rapport* presented to the Moscow Congress (314). He admits that the chromatic substance plays at the same time a considerable *rôle* in the nutrition of the cell. There seems every reason to believe that both of these views are essentially accurate.

Lugaro (250) expressly states that he believes that the chromatic substance has an important and indispensable part in functional metabolism of the nerve-cell. Bevan Lewis (272), in stating that "Lugaro regards Nissl's granules, so far as function is concerned, as having a passive rôle," has unwittingly misrepresented the view of the Italian neurologist, whose use of the term "passive" in this connection has reference not to function, but to the morphological relationship of the chromatic substance to the achromatic fibrils (Lugaro, 239-250). The contention of Goldscheider and Flautau (165), that the Nissl-bodies have no vital importance for the nerve-cell, has been fully answered by Lugaro (250) and Marinesco (327).

The histological evidence that the chromatic substance is utilised during functional activity of the nerve-cell was for long of a somewhat unsatisfactory kind, but Pellizzi's recent observations upon the changes in the cells of the cœliac and mesenteric ganglia during digestion (see Section I., 11) furnish what is probably the most important evidence that has yet been obtained in confirmation of the conclusion of Mann formulated in 1894.

The great majority of authorities are agreed that the fibrillar portion of the achromatic substance subserves the function of conduction of the nervous wave. Cajal (433), however, considers that we are not warranted in restricting the performance of this function to a single structural element. The non-organised portion of the achromatic substance is believed by Marinesco (322) to be the seat of intense chemical phenomena, and of such importance for the nervous element as to be appropriately designated the *trophoplasm*. That this substance is the seat of important metabolic changes is amply confirmed by other observers, more especially by Giuseppe Levi from his study of the fuchsinophile granules.

Functions of the Cell-Body.—The cell-body in virtue of the fact that it contains the nucleus is clearly the trophic centre for the whole cell-element. That this is so is fully borne out by experimental evidence. But there seem to be the strongest reasons for believing that the cell-body has also other special functions to perform, although there are some authorities who would limit its rôle to that just stated. According to the law of dynamic polarisation, the nervous wave is received by the terminations of the dendrites, carried to the cell-body and thence to the axon. Now, according to the views of the best authorities on the subject, this nerve-wave, arriving at the cell-body, is there essentially modified and reinforced before being discharged by way of the axon. This is the teaching of the two Continental neurologists who have given most attention to the question, and who, from the vast range of their experimental observations, have the best title to be heard upon it. I refer, of course, to Marinesco and Lugaro.

Marinesco's theory of the function of the chromatophile elements, already noticed, implies that in the cell-body the nerve-wave has its potential energy largely increased in virtue of the chemical changes which occur in these elements. He further states (314), "it is due in part to the modifications which the chromatophile elements impress upon the nervous wave that the nerve-cell becomes a source of energy. . . . . The mechanical conception of the nervous phenomena which I have just formulated in this work is in harmony with many physiological and pathological phenomena. In fact physiology teaches us that the nerve-cell is a source of energy, and this source of energy, according to my view, is due at least in large part to the modifications which the chromatophile elements impress on the nervous wave which traverses the cell." In other papers he is no less explicit in maintaining that in the body of the nerve-cell there takes place a liberation of energy which serves to augment the nerve current as it traverses the cell. Lugaro's opinion upon this subject has also been often and clearly expressed.

I need quote only one passage :—" From facts regarding the structure of the cell-body it is seen that this is not a simple conductor but a modifier of the nervous wave, whence the necessity of the afferent current traversing it in every case before passing in a modified form to the efferent prolongation " (247a).

The recent teaching of Gowers (182) upon this point is doubtless well known to the reader. His opinion that the fibrils " can merely conduct through the cell-body as they do elsewhere in their course," in other words that the cell-body does not generate nerve force, is one that is doubtless shared by other neurologists, but the fact remains that the great weight of authoritative opinion is at present entirely against it.

The alleged amœboidism and plasticity of the nerve-cell.—Attention has recently been directed at considerable length to the present position of this important question by the *British Medical Journal* (67). I can only refer to it here very briefly. A large number of observers, chiefly belonging to the French and Belgian schools, have maintained, partly from experimental evidence, partly upon purely theoretical grounds, that the protoplasmic prolongations of nerve-cells exhibit functional contractility. They maintain that contraction of them occurs in fatigue of the nerve-cells, and that it is capable of explaining sleep, hysteria and many other cerebral phenomena. Lugaro (252), on the basis of a series of entirely new experiments, denies that the processes of nerve-cells contract to any important extent in different functional states, that on the other hand it is only the gemmulæ that undergo movements of retraction and propulsion, and that not retraction of these processes, but general expansion of them, is characteristic of sleep. His experimental results, obtained with the aid of an incomparably superior technique, certainly go far to prove that the histological evidence of contraction of the protoplasmic processes obtained by other observers is entirely fallacious. In connection with this subject it deserves to be mentioned that the fresh method of Turner (492) gives a beautiful demonstration of the elasticity of the nerve-cells. But it is, of course, impossible to affirm that this elasticity postulates anything as to their functional plasticity.

It may be useful to give here an index of the papers included in the list of literature which deal with this subject :—518, 489a, 445, 127, 274, 398, 120, 121, 228, 424, 433, 107, 108, 3, 417, 188, 189, 451, 389, 474, 125, 356, 215, 252, 168, 67.

Primary and secondary lesions.—Marinesco (305-312-314) has maintained that the changes that occur in a nerve-cell after section of its prolongation (secondary lesions) have a special character which permits of their being distinguished from those that occur from the direct action of a noxious agent (primary lesions). In secondary degeneration the nerve-cell always comports itself in a uniform manner. The alteration begins by disintegration of the chromatic substance in the neighbourhood of the cone of origin of the axis-cylinder process, and gradually extends to the greater part of the cell-body. At an advanced stage the nucleus is often displaced to the periphery. The cell may undergo repair, or it may atrophy and disappear. In primary degeneration the alterations are specially characterised by their variable multiplicity and by their gravity. The chromatolysis may be partial or complete, peripheral, perinuclear or diffuse, &c. The achromatic substance and the nucleus tend to be involved, and repair is then rendered impossible.

Further experience of secondary lesions has shown that the alterations are not so characteristic as was at first proposed. Some observers have been unable to see any differences in the two classes. Nevertheless, there seems to be little reason to doubt that secondary lesions have features distinctive from primary lesions. If present investigation cannot fully confirm Marinesco's contention, those of the future may be trusted to do so.

Degeneration by transmission, or secondary neural atrophy.—Some discussion has lately taken place regarding to what extent the degeneration of one neuron involves the degeneration of another to which it normally transmits its functional impulse. Jelgersma (219) and Klippel (232) have described the occurrence of such "degeneration by transmission." Marinesco (302-306) maintains that trophism is a reflex action propagated from one neuron to another, and that continued functional excitation is indispensable to trophic activity in the nerve-cell. He points to examples of what he terms "secondary neural atrophy" of nerve-cells in the human subject as the result of degeneration of the cells from which they normally receive stimuli. K. Schaffer (464) has attributed the degeneration of the cells of the anterior horn of the spinal cord in amyotrophic tabes to degeneration of the collaterals of the posterior roots, and the consequent loss of the stimuli normally received from them. He has also observed degeneration of these cells in cases of hemiplegia from cerebral lesions. Van Gehuchten (169) attaches great importance to the trophic influence that one nerve-cell exercises over another. He records some experimental observations which go to show that after section of the sensory nerves the histological alterations do not confine themselves to the first neurons, but affect also the second which are in connection with them. He thinks that this degenerative process may pass on to neurons of the third order, and even be transmitted to the motor neurons. Berger (53) found no change in the cells of the cord three weeks after extirpation of the motor region of the brain. Acquisto and Pusateri (17), in a case of amputation of the leg, observed after twenty-nine years degeneration and loss of nerve-cells in the corresponding area of the motor cortex. Warrington (522) observed chromatolytic changes specially in the postero-external group of cells of the anterior horn of the spinal cord after section of the posterior roots, and attributed them to withdrawal of the afferent impulses which normally impinge on the cornual cells. K. Schaffer (466) found similar alterations of this group of nerve-cells in a case of cerebral hemiplegia of short duration, and regarded them as consecutive to degeneration of the pyramidal tract. Lugaro (257a) believes that these cells are sensory neurons of the second order, and thinks that their degeneration in Schaffer's case may perhaps be explained by injury to their ascending prolongations in the brain. It must not, however, be inferred from this that Lugaro denies the occurrence of degeneration by transmission.

In concluding this digest, I desire to express my indebtedness especially to Dr. Clouston, Dr. Alexander Bruce, Dr. D. A. Welsh, Dr. W. R. Dawson and Dr. Harry Rainy for the kind assistance they have given me in getting access to literature.

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Review.

The Medical Jurisprudence of Insanity or Forensic Psychiatry. 2 vols., 8vo, pp. 1356, 1898. The Lawyers' Co-operative Publishing Company. Rochester, New York.

THIS ambitious work is, as the author tells us in his preface, an attempt to unite a general medical text-book upon insanity with a medico-legal treatise and a digest of the English and American law to meet the requirements of lawyers and physicians in civil and criminal cases.

The scope of the work is very wide. It comprises definitions, classification, symptoms and diagnosis as the medical part of the first volume, followed by reports of criminal cases, legal adjudications in criminal cases, civil cases and legal adjudications in them, and an important chapter upon evidence of insanity, concluding with a chapter on the competency of witnesses and jurors.

The second volume treats of alcoholism, the legal consequences of it, and the decisions of the Courts upon it, together with a chapter on Morphinism, and other addictions and many other subjects, among which we may mention Degeneracy, Hysteria, Epilepsy, &c., and concludes with chapters on Etiology, Prognosis, Pathology, and treatment. As will be seen by this rapid survey, the work covers an enormous amount of ground. The author handles his subject in a clear and comprehensive manner, and has succeeded in giving to the profession as the result of his great labour a valuable and reliable medico-legal treatise upon what he terms "Forensic Psychiatry."

T. OUTTERSON WOOD, M.D.

BRAIN.

PART III., 1899.

Original Articles and Clinical Cases.

ON THE MEANING OF THE CRANIAL NERVES.

BY W. H. GASKELL, M.D., LL.D., F.R.S.

Being the Presidential Address to the Neurological Society for the Year 1899.

ELEVEN years ago, in 1888, I read a paper[1] before the Neurological Society on the origin of vertebrates. In that paper I gave the conclusions to which I had come on the nature of the central nervous system of vertebrates. Since that time further and further work has only confirmed me in those conclusions and led me to more and more definite explanations of the meaning and origin not only of the brain but also of the cranial nerves and their distribution. That paper was the direct outcome of previous work on the peripheral nervous system, especially the sympathetic nervous system,[2] which led me to attempt to formulate to my own mind the nature of a segmental nerve, and the comparison therefore of the cranial and spinal nerves both as regards their structure and the function of their component fibres. I came to the conclusion that the spinal nerves contained the same elements as the cranial segmental nerves, but that these elements were grouped together differently; in the former case being grouped into the two great divisions of dorsal and ventral or sensory and motor

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[1] BRAIN, vol. xii., p. 1.

[2] *Journ. of Physiol.*, vol. vii., p. 1, 1885.

roots; in the latter being divided into three rather than two groups, viz., dorsal, lateral and ventral. Of these three roots the dorsal and ventral groups corresponded to the spinal nerves in that they were sensory and motor respectively, while the lateral group was something different, being mixed in function, both sensory and motor. Further, having regard to the anatomical work of Charles Bell and the embryological work of v. Wijhe, it was clear that this tripartite grouping of the cranial nerves was in reality an expression of a bipartite grouping, not however as in the spinal nerves into motor and sensory, but corresponding to the double segmentation of the head region into splanchnic and somatic; I came, therefore, to the conclusion that the cranial segmental nerves consist of a series of segmental nerves the somatic elements of which are arranged like those of the spinal nerves into dorsal and ventral, *i.e.*, sensory and motor groups—such elements being on the one hand the ascending root and somatic sensory portion of the trigeminal nerve, on the other the nerves to the eye muscles and the hypoglossal nerve—while the splanchnic elements form well-defined single nerves which are mixed in function, viz., the vagus, glosso-pharyngeal, facial and motor part of the trigeminal nerves, together with the sensory splanchnic portion of the trigeminal. The question therefore, immediately arose, which method of grouping must be considered the most primitive, the spinal or the cranial. So much are we the slaves of fashion, so powerful has been in the past the influence of the theory of the origin of the skull from modified spinal vertebræ, that almost all the attempts to solve the origin of the cranial nerves have started with the assumption that they arose from the modification of spinal nerves, which were built up originally on the same plan as the existing spinal nerves; that therefore, as a logical corollary, the brain region of the central nervous system has arisen from the modification of a spinal cord type of central nervous system.

In this Society I have little doubt what answer will be given to the question, where did the central nervous system commence? Surely the oldest part of us is that part of the brain mass which was concentrated around the organs of special sense at the anterior end of the body.

Throughout the whole animal kingdom as soon as a definite central nervous system is formed we find it in the shape of an oral ring of specialised nerve matter, concentrated around the mouth in connection with special sense organs for the purpose of gaining food. Again and again embryology shows that the head region with its nervous centres is the first formed, and the body region is a subsequent formation; this is especially manifest in those animals which, like the vertebrate, possess an elongated segmented body, and we see how the subsequently formed nerve-centres of the elongated body are subservient to the first formed centres in the head. Every consideration, every argument as pointed out in my paper in the *Journ. of Anat. and Physiol.*, vol. xxxii., p. 547, forces us to the conclusion that the cranial region is older than the spinal, and that therefore, in endeavouring to find out the meaning of the cranial nerves, we must not attempt to derive them from a pre-existing spinal type of segmental nerve, but on the contrary, the type from which both cranial and spinal nerves have arisen must have resembled the existing cranial type more nearly than the spinal.

What evidence, then, have we as to the nature of the cranial nerves? In all attempts to read the past history of segmental nerves by means of the anatomical and physioogical investigation of existing types, it is of paramount nportance to consider, not only the exit from the central rvous system and the peripheral distribution of the arate nerves, but also their origin in the central nervous tem, especially, therefore, the nuclei of origin of their tor nerves. In considering this question we are struck h two facts of marked significance; in the first place the tres of origin of the motor nerves fall into two distinct groups, viz., a lateral group of nuclei forming the centres of origin of the nerves V., VII., IX., X. and XI., and a more dorsally situated group of nuclei from which arise the nerves III., IV., VI. and XII.; in other words, the nuclei of origin of the motor cranial nerves separate into two well-defined splanchnic and somatic groups in exact correspondence with their peripheral distribution. In the second place, the motor nuclei of the cranial nerves are much more markedly separated from each other than is the case with the corresponding nuclei of the spinal nerves; in the latter case the nerves are clearly segmental, but their centres of origin are not so clearly segmental; in the cranial region, however, the different motor nuclei are well defined and separate.

Both these facts lead directly to the conclusion that that part of the brain which gives origin to the cranial segmental nerves was formed by the concentration and fusion of a number of separate segments or ganglia, each of which originally gave origin to nerves innervating a segment composed of two parts, viz., a splanchnic or branchial part and a somatic part. The anatomical and physiological evidence is overwhelming that the vertebrate central nervous system is built up of a series of segments or ganglia fused together.

The next fact that is forced on the attention is the arrangement of these nerves along the axis of the brain. The brain region may be divided into two portions in accordance with the position of the notochord—a prechordal and an epichordal part, and, as is well known, the epichordal region of the brain alone gives origin to these nerves, its anterior limit being fixed, not only by the termination of the notochord, but also by the presence of th tube of the infundibulum, while posteriorly it merges int the spinal cord and so connects the spinal cord system wi the cranial system.

Further, this system itself falls into two well-mark regions, an anterior or pro-otic region, which gives ori to the trigeminal and eye-muscle nerves, a region theref connected with mastication and movement of the eyes, a posterior or opisthotic region, which gives origin to vagus group of nerves, a region therefore connected e cially with respiration.

Throughout the vertebrate kingdom down to the l true vertebrate such an arrangement is most constan fixed.

It is therefore certain that the anterior limit of this epichordal part of the brain, which gives origin to these segmental cranial nerves, is invariably fixed by the presence of a prolongation of the central tube of the nervous system, which extends right to the ventral surface and is known by the name of the tube of the infundibulum. On each side of this tube lie the crura cerebri which connect the prechordal portion of the brain with the epichordal, and we know that from this prechordal part of the brain nerves also are given off, but they are of a special kind, differing from the epichordal nerves in that they are nerves of special sense—the olfactory and the optic.

In other words, our search for the meaning of the cranial nerves pictures to us an animal with a specially developed anterior or supra-infundibular brain mass, the cerebrum proper, which gives origin only to olfactory and optic nerves, connected by two massive infundibular commissures, the crura cerebri, with an infra-infundibular brain mass, which gives origin to a series of segmental cranial nerves, whose members fall naturally into an anterior group connected with mastication and a posterior group connected with respiration.

These facts, about which there can be no dispute, point directly to the conclusion that the type of nervous system which gave origin to the vertebrate brain is identical with the type of nervous system in the great appendiculate group of invertebrates, *i.e.*, to the type of nervous system in the highest invertebrate group; for there, too, we see that a pecially developed most anterior part of the central nervous stem or supra-œsophageal brain mass—the cerebrum oper—which gives origin only to olfactory and optic nerves, connected by the two œsophageal commissures with an ra-œsophageal brain mass, formed in the higher inverte- e groups by the fusion of the separate ganglia, which s origin to a series of segmental nerves whose members naturally into an anterior group connected with mastion and a posterior group connected with respiration.

nly difference between these two types of brain is be around which the whole brain mass is grouped is called in the one case the infundibular tube, in the other the œsophagus.

The natural and rational conclusion from such a striking coincidence is that the tube of the infundibulum represents all that remains of the original œsophagus, and that therefore the vertebrate, together with its poor relation the tunicate, fall into line with the rest of the animal kingdom, in that its central nervous system was formed originally by the modification of an oral nerve ring.

But the cavity of the tube of the infundibulum is continuous with the cavity of the third ventricle and, therefore, with the central canal of the nervous system, and its epithelial lining is continuous with the epithelial lining of the tube of the central nervous system. There is no discontinuity, no sign whatever of the presence of the remnants of any œsophageal tube separate from the central tube itself; no evidence, in fact, that it is possible to look upon the infundibulum as the remnant of the œsophageal tube, as Dohrn and others have done, which passed between the crura cerebri and terminated in a mouth which was situated on the present dorsal surface of the animal; the dorsal surface of the vertebrate on this view having been originally the ventral surface of the invertebrate. On the contrary the evidence of continuity is so conclusive that it becomes a logical certainty that if the tube of the infundibulum was the original œsophagus, then the ventricles of the brain must have been the original cephali
stomach into which the œsophagus opened and the can
of the spinal cord with its termination in the anus by mea
of the neurenteric canal, the straight intestine which
direct from the cephalic stomach to the anus in
invertebrate.

The search then for the meaning of the cranial ne
has led me by the strong logic of incontrovertible facts t
conclusion that the central nervous system of the verte
is composed of two parts, a part which is nervous a
arranged segmentally, and a part which is non-nervo
composed of an epithelial tube on the outside of
nervous material has been grouped, and, owing t

the remnant of the alimentary canal of the invertebrate, is not composed of segments.

This, then, is my working hypothesis, and the value of it depends essentially upon its power to explain or to elucidate the whole mass of problems connected with the origin of vertebrates. Its very essence is that it explains that most striking and otherwise unaccountable tubular nature of the vertebrate central nervous system, and this explanation is of such a character as to afford a test of its accuracy by the consideration of the phylogenetic development of the central nervous system in the vertebrate phylum alone, without making any guesses as to the nature of the passage from the invertebrate to the vertebrate; for it is clear that, if the brain region of man has arisen from the lowest fishes by the gradual increase of nervous material around an epithelial tube, then, as we pass lower and lower in the vertebrate phylum, we must find clearer and clearer evidence of the separate existence of that epithelial tube; while, on the other hand, if the tube of the nervous system was originally a nerve tube proper and not composed of two parts, as various embryologists assert, then the lower we go down, the more clearly ought the nervous character of that tube to come out and the less ought it to show a non-nervous, purely epithelial structure.

The evidence of comparative anatomy is absolutely conclusive on this point. Think of the growth of the cerebral hemispheres over the epithelial pallium of the fish as we pass upwards by way of the amphibians and reptiles to the higher mammalia; see how the cerebellum from its small eginnings in Ammocœtes forms first the worm and then by rther invasion of the epithelial roof the cerebellar hemieres;[1] think of the brain of Protopterus, of Lepidosiren of Ammocœtes (fig. 2) with the whole of its dorsal roof he epichordal portion composed of fold upon fold of branous epithelium except just where the fourth nerve the commencing cerebellum crosses over. Compare ictures (fig. 1) of the brain of the different classes, culminating in the brain of Ammocœtes.

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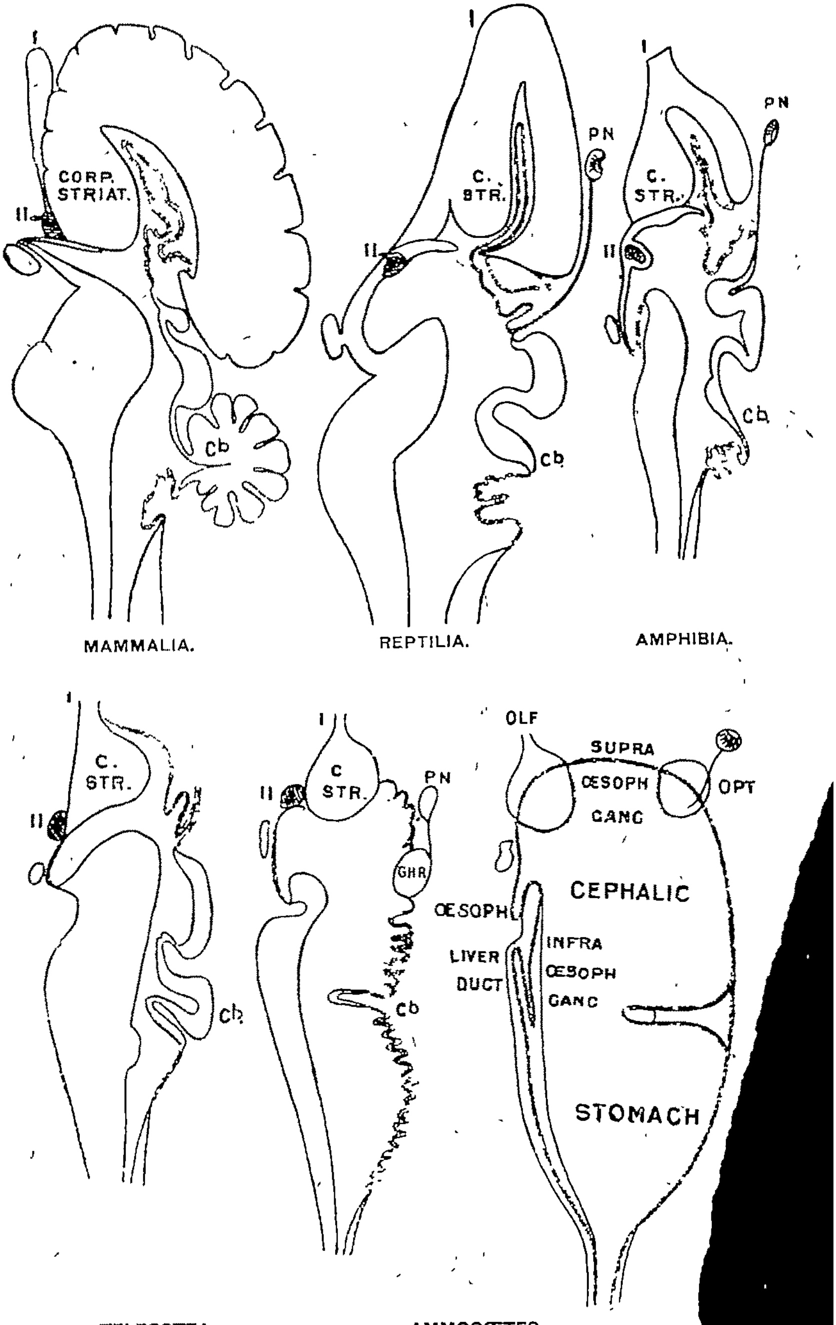
[1] *Journ. of Physiol.*, vol. x., p. 194.



MAMMALIA. REPTILIA. AMPHIBIA.

TELEOSTEA AMMOCŒTES.

Fig. 1.

Comparison of vertebrate brain from Mammalia to Ammocœte
parts represented by dotted lines; the last figure represents
Ammocœtes with the epithelial folds unfolded.

Is it possible for the evidence to be stronger that the nearer we get to the origin of vertebrates the more clearly does the separation of the nervous matter from the epithelial tube become apparent; other evidence to the same effect is at hand. Let me recall to your memory the formation of the rhomboidal sinus[1] in the lumbo-sacral region of the spinal cord in birds, the continuation of the canal into the regenerating tail of the lizard,[2] the pathological evidence of cystic malformations, all pointing to the conclusion that the central canal is of a non-nervous nature.

In absolute accordance with the evidence of the gradual separation of this epithelial tube from the surrounding nerve masses, as we descend the vertebrate phylum, is the evidence of the simplification of the nerve masses themselves, so that at last when we reach the Ammocœtes we find, as is seen in fig. 2, that the whole cerebrum is practically reduced to the basal ganglia, the corpus striatum, and optic thalamus, with the olfactory and optic nerves; reduced, in fact, to a supra-infundibular brain mass, which is directly and closely comparable with the supra-œsophageal brain mass of the higher arthropods. As the crowning fact of this evidence, a fact which is almost proof positive of the truth of my hypothesis, we find, in precisely the place where they ought to be, two median eyes, one of which is much better developed than the other; eyes which in the higher vertebrates have degenerated into the so-called pineal gland, but, as ought to be the case, show most clearly their invertebrate ancestry in that lowest of vertebrates—Ammocœtes—n which animal the structure of the right pineal eye clearly sembles one type of arthropod eye.[3] From the time when irst stated to this Society[4] the arthropod nature of the eal eye up to the present time, no better explanation has offered; the facts which I put forward have not been ted, but only ignored; and Leydig[5] has come to the

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urn. of Physiol., vol. x., p. 197.

indley, *Journ. of Bombay Nat. Hist. Soc.*, vol. ix., p. 1, 1894.

kell, *Quart. Journ. of Micr. Sci.*, 1890, fig. 20 a–d, plate XXVII. and XVIII.

AIN, *Op. cit.*, p. 14.

dig, "Das parietal organ der Amphibien u. Reptilien." *Abhand. d. berg. Naturforsch. Gesellschaft*, 1890, p. 588.

same conclusion as myself as to the arthropod character of this eye. If you picture to yourselves the supra-œsophageal ganglia of one of the higher arthropods your picture would take the exact form of the supra-infundibular brain of the Ammocœtes.

Equally striking is the physiological evidence, the functions of the supra-œsophageal ganglia correspond closely with those of the supra-infundibular, and the foremost

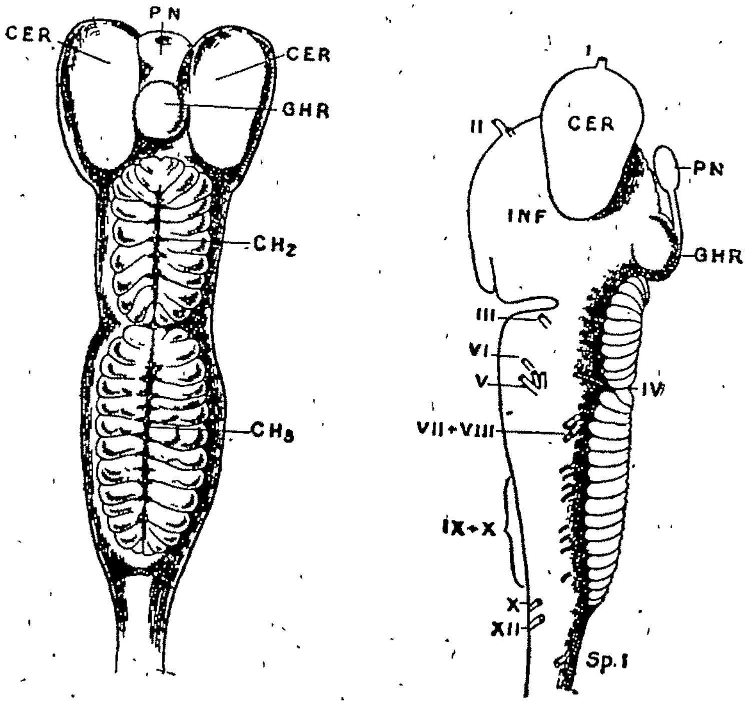

FIG. 2

Dorsal and lateral view of the brain of Ammocœtes. *CER*, cer hemispheres; *GHR*, right ganglion trabecula; *PN*, right pineal CH_2, CH_3, so-called choroid plexuses; *INF*, region of infundib *I.—XII.*, cranial nerves.

group of infra-œsophageal ganglia with their ma ing and special co-ordinating mechanisms correspon the trigeminal region of the infra-infundibular part brain from which the co-ordinating machinery cerebellum and posterior corpora quadrigemina has s while the hindermost group with their respiratory centre and nerves to the respiratory appendages correspond with the vagus region of the brain.[1]

Just as the study of the comparative anatomy of the vertebrate brain has led us gradually down to a brain mass like that of Ammocœtes directly comparable with that of an arthropod, so the study of the comparative anatomy of the arthropod brain points directly to the way in which such a brain as Ammocœtes was probably formed from the original annelid type. In all arthropods the foremost infra-œsophageal ganglia are concerned with the innervation of mouth appendages—these ganglia we may call prosomatic—between these and the abdominal ganglia we find a set of ganglia usually concerned with the respiratory appendages which may be called mesosomatic, then comes the most posterior group which may be called metasomatic. A series of diagrams to represent the arrangement of these prosomatic and mesosomatic ganglia in different arthropods, Branchipus, Astacus, Limulus, Scorpio, Androctonus, Thelyphonus, as given in fig 3, show how by a steadily progressing concentration and cephalisation, first the prosomatic ganglia (A) are fused into a compact infra-œsophageal brain mass, and then in the scorpion tribe more and more of the mesosomatic ganglia (B) become fused into this mass, until at last in the Pedipalpi such as Thelyphonus all the mesosomatic ganglia have fused to form a large brain mass and now the infra-œsophageal portion of the brain is directly comparable with the infra-infundibular portion of the Ammocœtes brain.
ere then the facts of the comparative anatomy of the
ertebrate central nervous system show how easy it is to
by slow gradation from the simplest central nervous
m of the lowest annelid direct to a brain like that of
ocœtes, just as the facts of the comparative anatomy
vertebrate nervous system have shown how easy it
ass by slow gradation from the highest brain of man
rain of the same Ammocœtes.

n a study of comparative anatomy points to a con-

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fuller statement of the physiological evidence, *cf. Journ. of Anat*
ol., vol. xxxii., pp. 582-587.

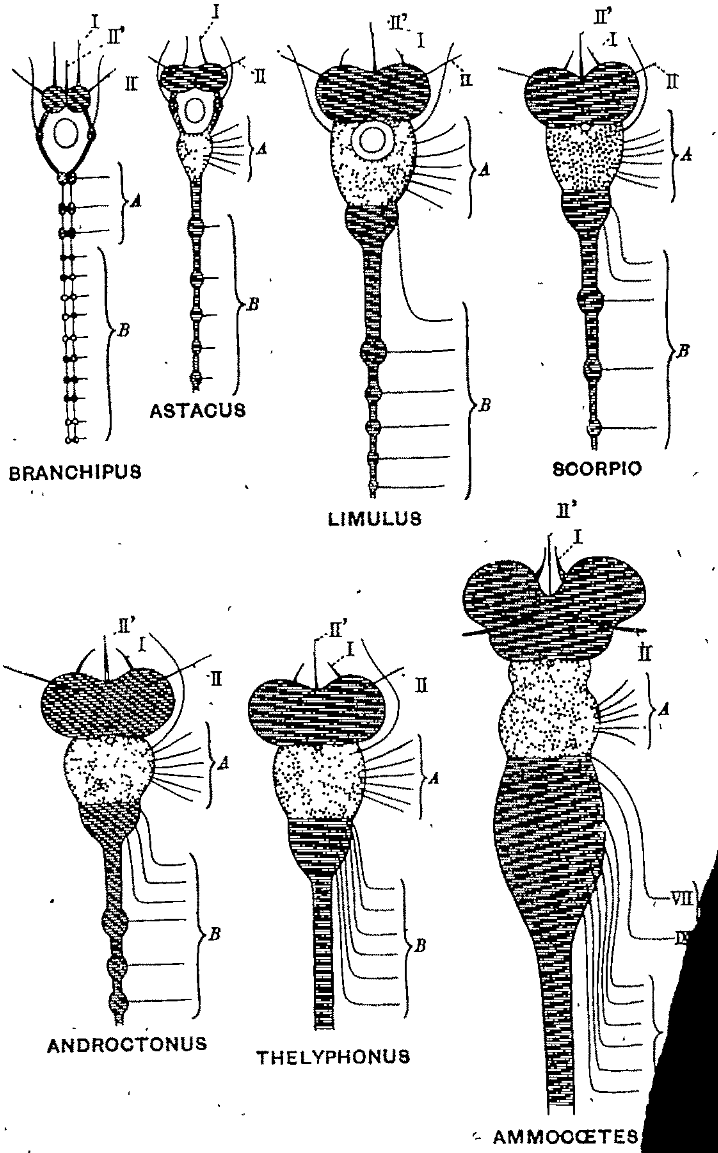

FIG. 3.

Comparison of invertebrate brain from Branchipus and Ammo clusion of great significance and immense importance for the whole theory of evolution, viz., that upward progress means increase of growth of nervous material, means concentration of nervous material, means cephalisation of nervous material. It is the brain which constitutes the evolutional power of the animal, it is the growth of the foremost part of the central nervous system, the concentration and cephalisation of the lower ganglia, so as to become part and parcel of the foremost mass which makes the brain.

That is the banner under which I fight, viz., that one organ or another may become rudimentary, may disappear or play a subordinate part, but throughout all the changes in the animal kingdom, no upward progress is possible which is accompanied with the degeneration or loss of the brain.

In our search then for the meaning of the cranial nerves, we are led in the first place to the direct conclusion that the prootic or trigeminal region of the brain was originally the prosomatic region of the brain, that therefore, the trigeminal group of nerves correspond to the prosomatic group, and that the opisthotic or vagus region of the brain was originally the mesosomatic region, so that the vagus group of nerves correspond to the mesosomatic group.

In the second place, we come face to face with a possible reason why the old alimentary canal ceased to function and the formation of a new alimentary canal became an absolute ecessity, for it is clear, if upward progress is possible ly by the growth and concentration of the brain nervous tter, that the scheme of piercing the brain with the phagus, which was a necessary corollary of a central ous system formed as an oral ring, must of necessity r or later lead to a deadlock, in which alimentation urther cephalisation would be antagonistic to each

he diagrams (fig. 3) you see how the lumen of the us becomes encroached upon with the increasing nd concentration of the brain, until at last in the s, Pedipalpi and spiders, the sole means of livelihood possible is by suction of blood, and as fig. 4 shows, the alimentary canal has become a mere central canal surrounded on all sides by the massive combined infra- and supra-œsophageal brain mass. Whether the growth of the brain is the cause of the diminution in lumen of the food channel and the consequent blood-sucking habits of the group, as to my mind is probable, or whether the blood-sucking habit has led to a diminution in size of lumen and the brain mass has then filled up the vacant space, the result in either case is to produce a group of animals in which the formation of a brain mass closely similar to t of Ammocœtes is correlated with an œsophagus of exc ingly small calibre; an œsophageal tube which is so n closed that its conversion into the infundibular tube no demand upon our credulity, but follows as a step, if the process of alimentation is otherwise p for.

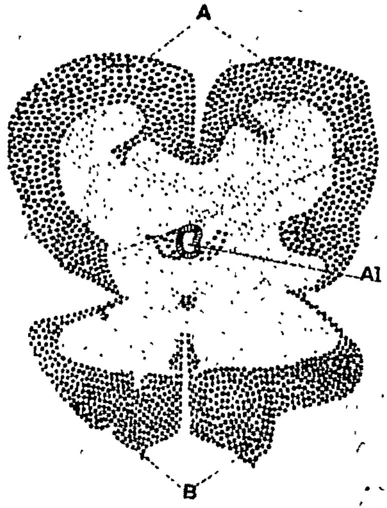

FIG. 4.

Transverse section through the brain of a young Thelyphonus. *A*, supr œsophageal ganglia; *B*, infra-œsophageal ganglia; *Al*, œsophagus.

Here we come face to face with the great difi this hypothesis of mine, which accounts most sati for the origin of the vertebrate central nervous system but necessitates the formation of a new food channel; how can we conceive that the new alimentary canal was formed?

I want you to dismiss from your minds all pre-conceived opinions and to follow out without prejudice the same line of argument as I have used hitherto, first of all bringing together the facts of anatomy and physiology, and then when they are arranged in line, forming your own opinion as to the conclusion to be derived from these facts. We have already seen that the epichordal portion of the vertebrate brain, divisible as it is into a trigeminal part and a vagus part, corresponds on our hypothesis with the prosomatic and mesosomatic portions of the brain of such animals as Limulus, Thelyphonus, &c., therefore it follows that the parts supplied by the vagus group of nerves ought to be the direct descendants of the parts supplied by the mesosomatic nerves, and the parts supplied by the trigeminal group of nerves ought to be the direct descendants of the parts supplied by the prosomatic nerves, and the closer the correspondence, both anatomically and structurally, the more likely is the theory to be true, the more clear shall we become as to the manner of formation of the anterior portion of the vertebrate alimentary canal.

The first problem to be decided is the following:—

The great characteristic of the cranial segmental nerves, s already mentioned, is that they fall into two sets for the pply of a series of splanchnic and somatic segments pectively, and that the splanchnic segments which in opisthotic or vagus group are always branchial, are lied by a series of separate nerves, mixed in function, arise as well-defined lateral nerves separately from orsal sensory and ventral somatic nerves. Conse- it follows that if the invertebrate motor nervous which gave origin to this type was of the nature rthropod nervous system, we ought to find in the d first, that a double segmentation of the body ich has impressed itself on the central nervous d secondly, that the nerves of each segment arise ots; of which the middle or lateral one is mixed in function, and supplies only the segments which carry the branchiæ or are serially homologous with these.

Now the observations of Hardy[1] have shown that the groups of nerve cells which form the separate ganglia of the central nervous system of Astacus, Branchipus, &c., are connected essentially with the segmentation of the appendages, and that the segments of the body are associated with quite distinct groups of central cells which are more diffuse and not confined to the separate ganglia, but spread along the connectives between the ganglia. In other words, there is a double segmentation here which has made its mark on the central nervous system, similarly to the double segmentation of the cranial region in vertebrates, and the two segmentations would agree if what I have called the splanchnic segments in the vertebrate had arisen from the segmental appendages of the invertebrate.

Further, we know from the work of Leydig and others that the segmental nerves of none of the invertebrata arise like the spinal nerves of the vertebrates from two roots which are respectively motor and sensory, but we do find that they do arise in many cases in a tripartite manner remarkably similar to the arrangement of the cranial vertebrate nerves.

Thus Milne Edwards[2] has given us a careful description of the prosomatic and mesosomatic nerves of Limulus, from which it is seen that the principal nerve of each segment i the large nerve which runs to the appendage of that segme and supplies nothing else except that appendage; this ne supplies the appendage with all its fibres both motor sensory. In addition to this appendage nerve two nerves arise from each of the ganglia, of which the on more dorsal one, is purely somatic sensory, supplyin its own area of the prosomatic and mesosomatic ca respectively (these nerves are called by Milne Edwa epimeral nerves); while the other is a small nerv supplies with motor fibres muscles, as Milne Edw it, not connected with the appendages, and may contain sensory fibres for the mid-ventral surface; a nerve root therefore which may be called somatic motor, with the possibility that it contains also some sensory fibres.

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[1] Hardy, *Phil. Trans.*, 1894, B., p. 83.

[2] "Recherches sur l'Anatomie des Limulus." *Ann. des Sc.*

Such an arrangement clearly corresponds to the arrangement of the cranial nerves of the vertebrates if the splanchnic segmentation was derived from the segmentation of the prosomatic and mesosomatic appendages, and the somatic segmentation was derived from the segmentation of the prosoma and mesosoma themselves. In other words the peculiarities of the cranial segmental nerves would receive an explanation in perfect harmony with my theory, if the structures innervated by the vagus, glossopharyngeal and facial nerves were derivable from modified mesosomatic appendages, and those innervated by the motor part of the trigeminal and its splanchnic sensory fibres were comparable with the modified prosomatic appendages; the somatic sensory part of the trigeminal with its ascending root would represent the epimeral nerves of the prosomatic and mesosomatic carapaces and the eye muscles all that remains of the somatic muscles of the prosoma and mesosoma. Conversely, if the tripartite arrangement of the cranial segmental nerves is due to the survival of the prosomatic and mesosomatic appendages in a modified form, then it follows that such an arrangement would give place to the dual system of the spinal cord by the simple dropping out of the appendage nerve; in other words if, as according to my view was the case, the system of appendages fashioned ke those of the arthropod was given up when the animal came a vertebrate, then, by the dropping out of the lateral ed nerves, the nerves would be arranged as in the spinal es of the present day; thus we can see how from the type of the cranial segmental nerves the type of the segmental nerves might naturally arise.

VAGUS NERVE GROUP.

owest vertebrate which possesses all the cranial d therefore allows of a direct comparison with the rves of the higher vertebrates, is the larval or

Ammocœtes form of the lamprey. The study of Ammocœtes, as pointed out in my papers in the *Journal of Anatomy and Physiology* (vols. xxxii. and xxxiii.), leads to

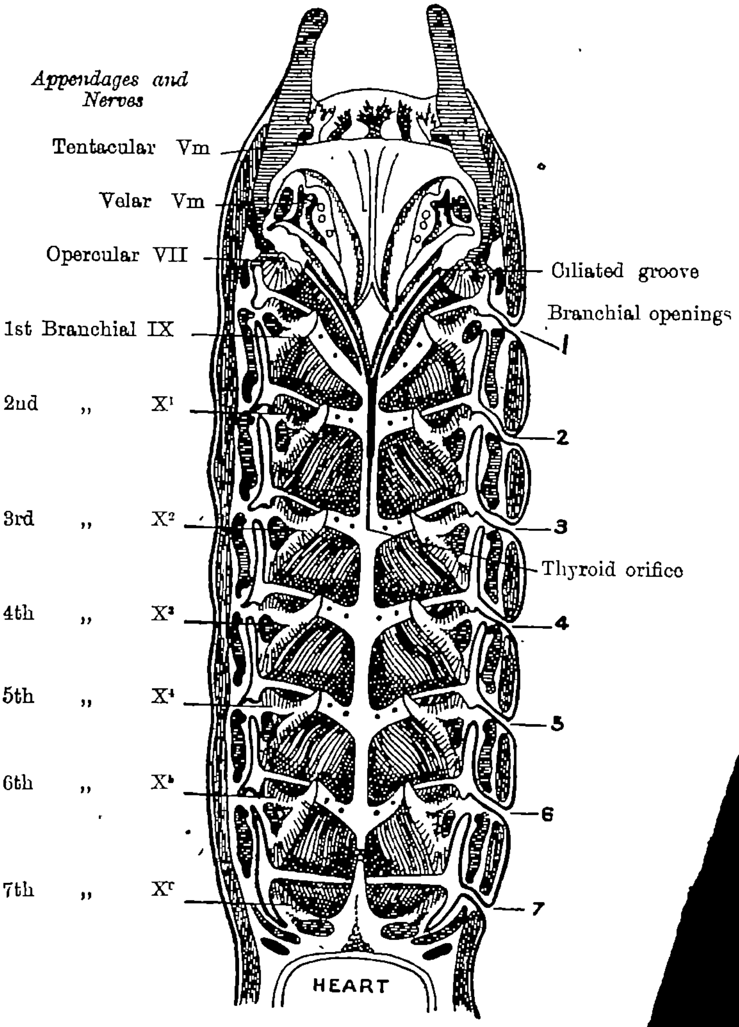

Fig. 5.

Head region of Ammocœtes, split longitudinally (ventral l

the conclusion that the mesosomatic respiratory a
of the scorpion-like ancestor still exist as the

bearing diaphragms of the Ammocœtes. As is seen in figs. 5 and 6, there are six complete pairs of diaphragms which bear branchiæ on both the anterior and posterior surfaces forming thus the sides of the respiratory chamber. This

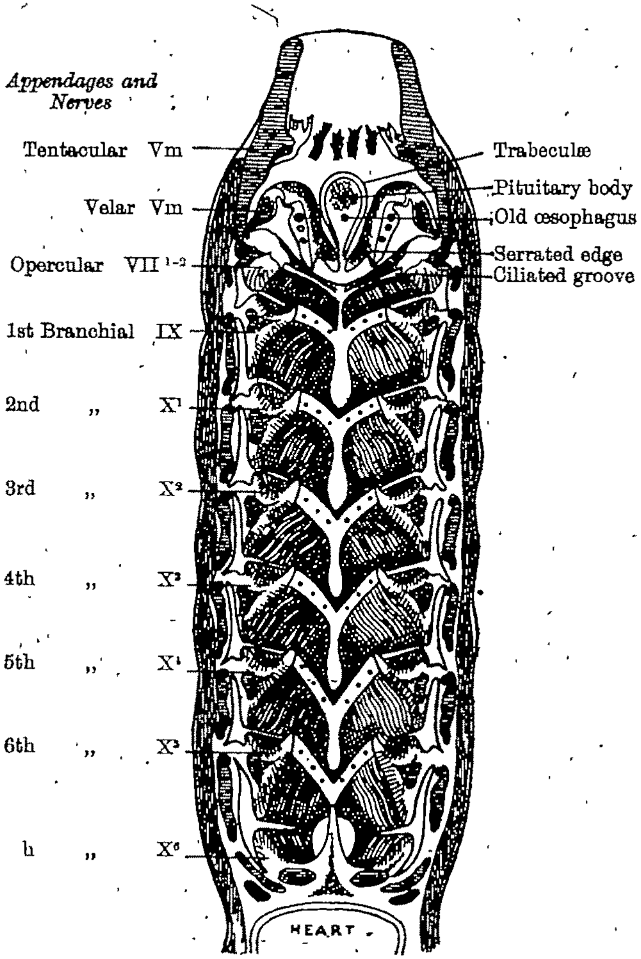

FIG. 6.

region of Ammocœtes, split longitudinally (dorsal half).

s completed by the last pair of diaphragms which hiæ only on one side and headwards by a pair ms which carry branchiæ only on one side, but bear as well the two ciliated grooves (Dohrn's pseudo-branchial grooves) which terminate ventrally in the thyroid gland. Each of the last six of these branchiæ-bearing diaphragms is supplied by a separate part of the vagus

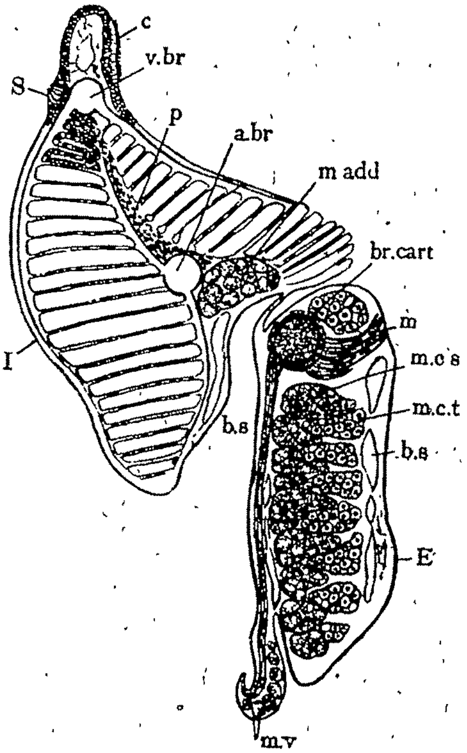

Fig. 7.

Section through branchial appendage of Ammocœtes. *br. cart.*, branc cartilage; *v. br.*, branchial vein; *a. br.*, branchial artery; *b. s.*, blood sp *p*, pigment; *S*, sense organ; *c*, ciliated band; *E*, *I*, external and in borders; *m. add.*, adductor muscle; *m. c. s.*, striated constrictor m *m. c. t.*, tubular constrictor muscle; *m.* and *m. v.*, muscles of valve.

nerve and just like the mesosomatic branchial appe of Limulus such nerve supplies *only* this branchial age; similarly the glosso-pharyngeal is the nerve second branchial appendage. In fig. 7 I gave a through one of these branchial appendages, in make it quite clear to you what in my opini branchial unit in this primitive vertebrate. Fu as I have pointed out,[1] the structure of the branchial lamella in Ammocœtes and Scorpio is closely similar and more striking still, the branchial cartilaginous bars so characteristic of the vertebrate branchial segments have their exact counterparts, both structurally and topographically, in the cartilaginous bars of the branchial appendages of Limulus.

It is worthy of note here that the arrangement of the branchial chamber of Ammocœtes shows clearly that the vagus nerve is not a single nerve, but is formed by the fusion of six nerves, each of which supplies a branchial segment; in consequence however of the concentration which has taken place in the formation of the medulla oblongata the separate centres of origin of these six mesosomatic nerves have become fused together into one long centre, the vagus nucleus, so that the number of segments represented by the vagus is not estimated by the number of separate cell groups in the central nervous system so much as by its peripheral distribution and by its epibranchial ganglia; a fact which it is important to bear in mind when considering the meaning of the oculomotor and trigeminal nerves.

In our search for the meaning of the cranial nerves we come then to the conclusion that the vagus and glossopharyngeal nerves originated as the nerves to a series of mesosomatic branchial appendages similar to the branchial
ppendages of the scorpion group of animals, which them-
ves had been derived from a series of free moving
nchial appendages similar to those of Limulus. In the
mpanying three figures (fig. 8, fig. 9 and fig. 10,) I have
esented diagrammatically the appendages and their
s in the three types of animals, viz., in Limulus, in
terus and in Ammocœtes, and in order to clearly
e corresponding parts I have lettered the appendage
of Limulus and Eurypterus in terms of the nerves
mocœtes and conversely have divided the head
f Ammocœtes into two parts which I have called
and mesosoma, in conformity with those divisions
us and Eurypterus.

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urnal of Physiol. and Anat., *Op. cit.*, Parts I., II., III.

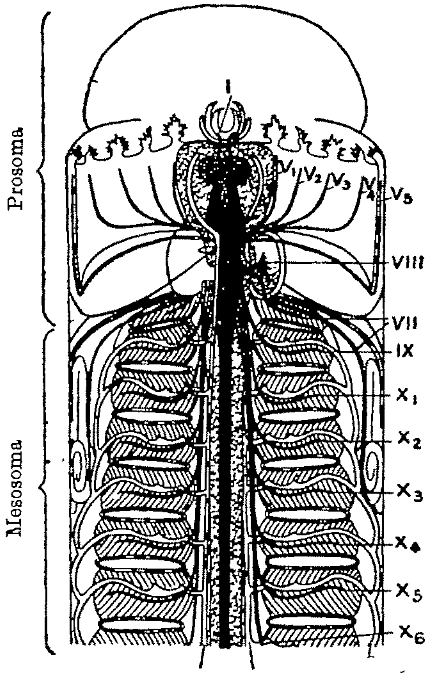

FIG. 10.

Ammocœtes. nerves of visceral segments and cartilages.

In all three figures V_1-V_5 = Prosomatic appendages and nerves; VII = 1st mesosomatic appendage or opercular appendage and nerves; IX, X_1 . . . = remaining mesosomatic appendages and nerves; M = chilaria in Limulus, metastoma in Eurypterus, corresponds to lower lip in Ammocœtes.

FACIAL NERVE.

The next cranial nerve which belongs to this series of esumed appendage nerves is the facial nerve, a nerve ch supplies the foremost of the branchial segments in ebrates, and ought, therefore, to have been derived from erve of the foremost mesosomatic appendage. Now we at in Limulus, in the Scorpions, in the Pedipalpi, the ost mesosomatic appendage is known as the operculum, fers markedly from the rest of the mesosomatic append- t consists in all cases of a pair of appendages fused r in the middle line, and in Limulus and the Scor- does not carry branchiæ but bears the terminations of the genital organs. In, however, the group of the Pedipalpi, Thelyphonus, Phrynus, &c., the operculum consists of a median portion which carries the terminal genital organs and a lateral posterior portion on each side which carries the branchiæ, as is seen in figs. 12 and 13. The operculum in these cases is, in fact, composed of the fusion of two pairs of segments, a paired branchial segment comparable to the other branchial segments, and a paired genital segment fused in the middle line, comparable to the operculum of the other forms.

The difference between the operculum of the scorpion group and of the Pedipalpi is shown in the figures 11, 12, 13, in all of which the limits of the operculum are indicated by dots. The corresponding segment in Ammocœtes, the facial segment, is shown diagrammatically in fig. 14, and also marked by dots; cross lines are drawn on the figure connecting the gill openings of each side so as to mark out the corresponding glosso-pharyngeal and vagus segments. The thyroid gland has been drawn as though it were two separate parts in order to indicate its bilateral character, in reality its appearance is as in fig. 15.

Apparently in the old extinct sea scorpions, Eurypterus, Pterygotus, Slimonium, &c., the operculum resembled that of the Pedipalpi rather than that of the Scorpion group, and in these forms the median genital part was frequently prolonged into a ventral tongue which extended over the first two or three branchial segments, as is shown in fig. 9, in which the limits of the operculum are marked out by dots.

What did this median tongue in all probability carry?
An answer to this question can be suggested only by findi
out what is carried by the median portion of the operculu
in the Pedipalpi or the whole operculum in the scorpio
These animals are without exception viviparous, and we
that in both sexes the paired genital organs termina
a single chamber which has been called in the scorpio
vagina, and in Thelyphonus the uterus. This u
chamber, as we may call it, is formed by the comi
gether and fusion of the genital ducts which were orig
as in Limulus, separate, and discharged by two se

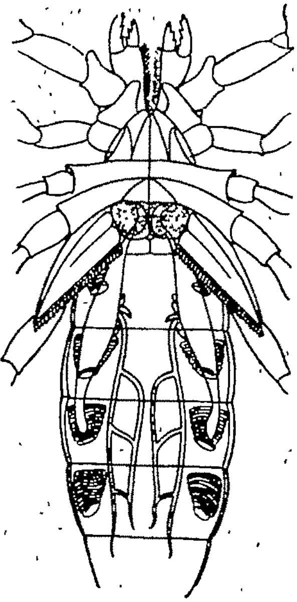

FIG. 11.—Androctonus.

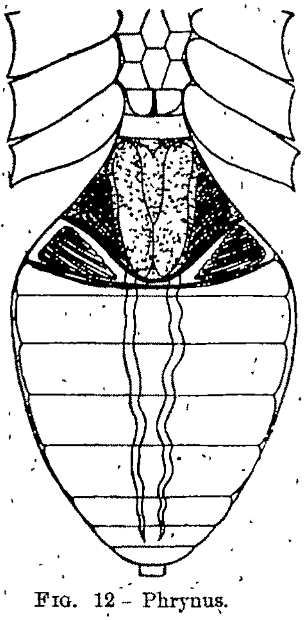

FIG. 12 – Phrynus.

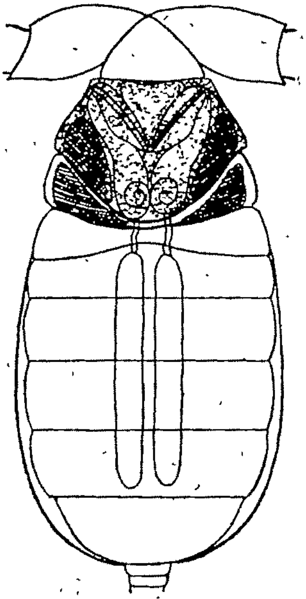

FIG. 13.—Thelyphonus.

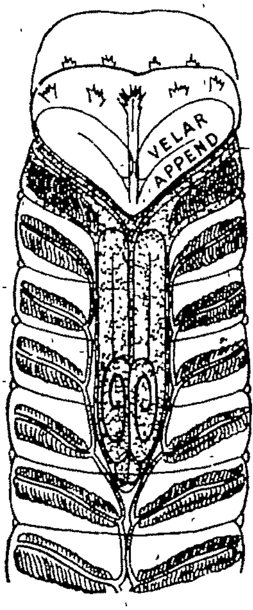

FIG. 14.—Ammocœtes.

openings. In the scorpions it opens directly to the exterior by an external orifice, but in Thelyphonus, according to Tarnani,[1] it does not open externally, but *internally*, by a large internal orifice into a chamber which he calls the genital chamber. This chamber is continuous with the pulmonary or branchial chamber on each side, so that the two opercular lung books or branchiæ are dependent into a common respiratory chamber into which also the products of the generative organs are discharged. Anteriorly the uterine chamber terminates in two horns which receive the genital ducts on each side.

An arrangement similar to this description of Tarnani existed in all probability in Eurypterus, so that we may imagine that the long median ventral flange of the operculum covered over an elongated uterine chamber.

If, then, as the whole argument seems to show, the ancestor from which such a vertebrate as Ammocœtes arose possessed many of the characteristics of these old extinct sea scorpions, it follows that the foremost pair of mesosomatic nerves, or facial nerves as they are called in Ammocœtes, ought to be found to innervate, not only the foremost of the paired branchiæ, but also an elongated median structure which might extend in the median ventral line at least as far as the second or third branchial segments, and might open into the branchial chamber and so indirectly to the exterior. This median structure ought to be composed of a long median chamber, in which we might expect to find evidence of its original formation from two tubes, terminating anteriorly in two horns, and possessing the structure of the scorpion uterus.

It is almost too startling to find that the segment which e facial nerve supplies in Ammocœtes is double, the terior or hyoid part being, like the glosso-pharyngeal and us segments, branchiæ-bearing, while the anterior and ian or thyroid part, which latter forms a median ventral e similar to that of Eurypterus, is not branchial in ion, but carries that unique organ, the so-called thyroid gland, and the two ciliated or pseudo-branchial grooves leading into it. Still more startling is it to find that this so-called thyroid gland is in reality an elongated chamber which opens by a large orifice (Th. o) into the same respiratory or pharyngeal chamber as the branchiæ project into. In fig. 15 I give a drawing of the thyroid of Ammocœtes. This large central chamber (C) of the thyroid which

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[1] rnani "Die genital organe der Thelyphonus" *Biol. Centralbl.*, vol 6, 1889.

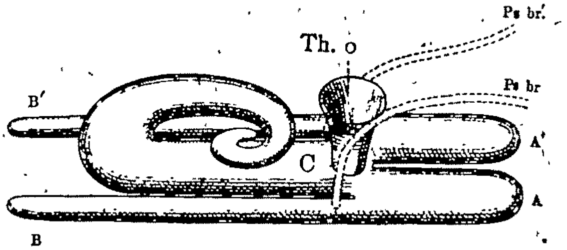

FIG. 15.

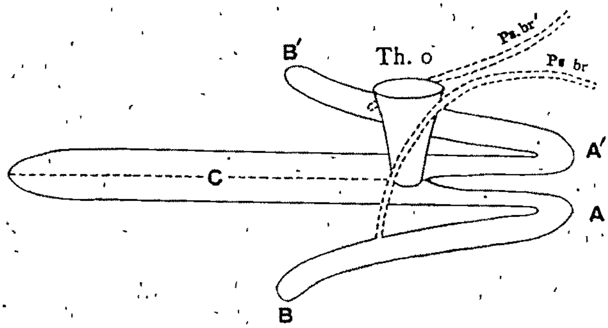

FIG. 16.

Figs. 15 and 16: thyroid gland of Ammocœtes. *C*, central chamber which divides anterior to the thyroid orifice (*Th. o*) into two parts, *A*, *A'*, continuous with the folded down horns, *B* and *B'*; *Ps br*, *Ps br'*, the two ciliate grooves, called by Dohrn pseudo-branchial grooves. In fig. 16 the curl portion of the central chamber is drawn uncurled and the two lateral hor *B*, *B'*, into which the ciliated grooves pass are slightly separated from central chamber.

is clearly composed of the fusion of two similar tubes, minates anteriorly into two separate tubes or horns which are folded down against the sides of the central and receive the terminations of the two ciliated or ps branchial grooves (Ps br.). If the curled portion thyroid be uncurled and the side tubes (B) separated from the central tube (C), then the appearance of the thyroid of Ammocœtes would be given by fig. 16, a figure which might well be a diagrammatic representation of the terminal genital or uterine chamber of a form like Eurypterus.

Finally, to complete the resemblance, the extraordinary character and arrangement of the cells forming the glandular tissue of this thyroid are found in the walls of the uterine chamber of the scorpion, as is seen in fig. 17, which represents a section through the uterus of the scorpion, and through the central chamber of the thyroid of Ammocœtes respectively.

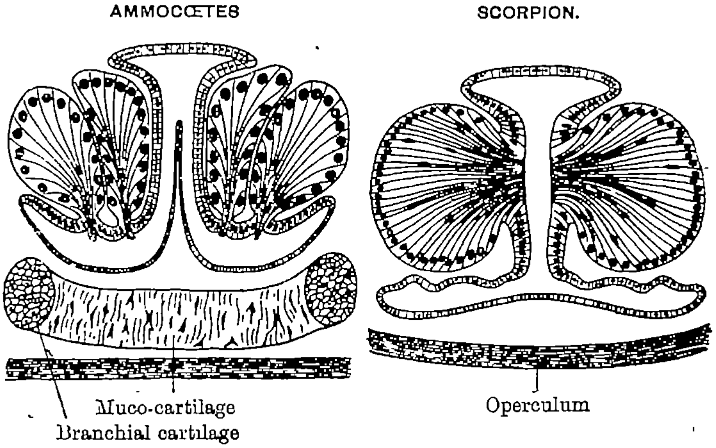

FIG. 17.

Section of central chamber of thyroid of Ammocœtes and section of terus of Scorpion.

Lastly, this remarkable and unique thyroid of Ammocœtes, gether with the whole of the thyroid segment, disappears transformation, showing by its existence only in the l stage that it is a relic of the past history of the race ot an organ of progressive development.

absolute harmony, then, with the origin of the central s system, is the meaning of the nerves of the medulla ata. Just as the medulla itself was formed according theory from the concentration of the mesosomatic so we see that the distribution of its nerves harmonises with that of the nerves of the mesosomatic appendages, the foremost of which was an operculum after the fashion of that of Eurypterus, and was supplied by the seventh nerve.

The evidence of Ammocœtes is conclusive that the seventh nerve belongs to the branchial system, *i.e.*, to the group of the vagus nerve and not to the trigeminal group.

TRIGEMINAL NERVE GROUP.

Turn now to the trigeminal nerve group, the group of nerves which according to my theory arose from the concentrated prosomatic ganglia, and ought therefore to have supplied prosomatic appendages, *i.e.*, appendages which did not bear branchiæ, but were used for tactile, prehensile and masticatory purposes. Such appendages, owing to their being serially homologous with the branchial appendages, and therefore supplied with serially homologous nerves, afford the reason why so many observers persist in endeavouring to find in this region primitive branchial segments.

Let us first consider the nature and number of these prosomatic appendages in the invertebrate. Throughout the arthropoda these foremost or prosomatic appendages form a well-defined group, the numbers of which are remarkably constant; thus we find in Astacus that immediately posterior to the two pairs of antennæ there are six pairs of prosomatic appendages, viz., the mandible, two pairs of maxillæ and three pairs of maxillipeds, or if the second pair of antennæ be included, seven pairs. In Limulus there are five pairs of locomotor masticatory prosomati appendages or foot-jaws immediately posterior to th chelicerae and a small abortive pair, the so-called chilari which Kishinouye[1] from embryological studies reckons a pair of true appendages; thus making six pairs prosomatic appendages posterior to the chelicerae, an the chelicerae be included, seven pairs.

In the scorpion, like Limulus, there are five pai locomotor prosomatic appendages posterior to the cheli according to Brauer[1] there is evidence in scorpions that another pair of appendages originally existed corresponding to the chilaria of Limulus, and Bruce[2] has described a form of Phrynus from the Bahamas, in which he states that something of the nature of chilaria is present.

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[1] *Journ. of Coll. of Sci.*, Tokio, vol. v., p. 72, 1891.

Undoubtedly in the extinct sea scorpions the chilaria were present in the form of a lower lip or metastoma, which was formed by the fusion and forward growth of the two chilaria, so that in this group a distinct prosomatic chamber was formed which contained five, or including the chelicerae, six prosomatic appendages. Further, the evidence of palæontologists is to the effect that these prosomatic appendages, which in Limulus were powerfully built for the purpose of tearing and masticating food, had dwindled more and more in the various sea scorpions, until as in Eurypterus they were represented by mere tactile appendages (fig. 9), which were all capable of retraction into the chamber formed by the metastoma and the hood, with the exception of the last pair which had become a locomotor swimming apparatus.

A still further continuation of the same process would lead to an animal which possessed only reduced tactile prosomatic appendages situated within an oral chamber formed by the forward growth of the metastoma or lower lip.

In fact, it is easy to conceive a condition of affairs arising closely resembling or even identical with what is found in Ammocœtes. Here we find, what is not found in other vertebrates, a large oral chamber, which contains a series of tactile organs, the tentacles. This chamber is rmed by the forward growth of the lower lip, and was iginally completely separated off from the respiratory amber by a septum, part of which forms the so-called um.

Such chamber is usually spoken of as the stomodæal gination, and the septum is called the septum of the odæum. Judging from the description given by Dohrn y Kupffer, this chamber is formed by the forward growth of the lower lip (as is shown in B, fig. 18), and not by any process of invagination. In this chamber are formed the tentacles, of which five on each side are especially conspicuous in the early stages, the median ventral one being formed by the fusion of a right and left pair. In addition to the tentacles we find also a large paired organ, the so-called velum, which contains blood, and fills up a large portion of the oral chamber; the muscles of the velum are of the tubular type and contract synchronously with the tubular respiratory muscles.

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[1] *Zeitsch. f. Wissensch. Zool.*, 1895, vol. lix

[2] Bruce, *Johns Hopkins Univ. Circular*, Dec., 1886, p. 47.

Strange indeed is the appearance of this primitive vertebrate in this region; stranger still to find that at transformation these tentacles and velar appendages disappear and give place to the remarkable suctorial apparatus of the adult form. Such a conversion of the appendages round the mouth into a suctorial apparatus is a common trick amongst arthropods. In accordance with all that has been urged before as to the meaning of the transformation I look upon these larval appendages as giving a clue to the past history of the animal, and therefore to the origin of the great trigeminal nerve of the vertebrate; for it is a significant fact that the muscles which the trigeminal nerve supplies in this animal are the muscles of the lower lip, the muscles of the two vela, the muscles of the tentacles and the muscles of the upper lip; the other muscles of this region, the longitudinal somatic muscles, which extend forwards nearly up to the nasal orifice, are supplied by spinal nerves, and the eye muscles by the third, fourth and sixth nerves.

I would suggest, then, that the motor part of th trigeminal is the representative not of a single nerve belon ing to a single splanchnic segment, but of the fusion of series of nerves belonging to six or seven segments whi were originally represented by the six or seven prosom appendages, viz., the five prosomatic locomotor appenda the metastoma or lower lip and the cheliceræ, jus undoubtedly the somatic sensory part of the trige belongs not to one segment but to a number of so segments.

Apart from the presence of tentacles and velum, the distribution and extent of the nucleus of the motor part of the fifth nerve is to my mind significant from this point of view; for it appears from the observation of Kölliker, Gehuchten[1] in the trout, Mayser[2] in Teleosteans, Lugaro[3] and Obersteiner,[4] well established at the present time, that the descending root of the fifth with its vesicular cells belongs to the motor part, so that the motor nucleus of the fifth extends from the very commencement of the segmental cranial nerves in the region of the beginning of the third nucleus down to the termination of the origin of the fifth in the region of the pons. In other words, just as ought to be the case, the motor nucleus of the fifth extends throughout the whole prosomatic region of the brain, though as might also be expected the foremost part of it has thinned down to the dimensions of the descending root. Examination of the arrangement of these cells on the descending root shows signs of grouping in places, as described by Mayser, but such grouping is not definite enough to enable us to come to any conclusion as to the number of segments represented in this descending group. It is also a most interesting fact to find that the most anterior of the cells of this root nearly meet in the middle line dorsal to the aqueduct of Sylvius, close to the posterior commissure; so that actually cells which give origin to part of an outgoing efferent nerve are situated on the dorsal side of the central tube. Such a situation of the foremost cells f the motor trigeminal nucleus is of special interest in onnection with the statement of Brauer[5] that the foremost osomatic ganglia in the Scorpion travel in the embryo m the ventral to the dorsal side of the tube of the entary canal.

The motor part of the trigeminal nerve in Ammocœtes almost be spoken of as arising from two roots, of which most posterior supplies the velum and the lower lip, while the most anterior splits into a series of separate branches for the supply of the tentacles and upper lip. The characteristic way in which the velar nerve turns abruptly forward to supply the lower lip, and that only (fig. 10),[1] inclines me to the belief that the velum and lower lip may belong more closely together than I originally thought, and it is worthy of consideration whether the formation of the metastoma from the chilaria of Limulus may not have originated the velum as well as the lower lip.

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[1] *Bull. de l'Acad. Sci Belg.*, 1895, 3rd Ser., vol. xxix

[2] *Zeitsch. f Wiss. Zool.*, vol. xxxvi., 1882.

[3] *Manitore Zool. Ital.*, vol. v., 1894, p. 171.

[4] *Nervose Central Organe*, p. 404.

[5] *Op. cit.*

It is, perhaps, worth mentioning here that Kupffer, in his recent papers on the embryology of Ammocœtes, considers from the evidence of the so-called epibranchial ganglia that the trigeminal nerve is formed by the amalgamation of at least five segmental nerves.

A further and very important clue in the unravelling of the trigeminal group of nerves is afforded by the consideration of the third, fourth and sixth nerves.

EYE MUSCLE NERVES.

All observers are agreed that the oculomotor and trochlearis nerves belong to the trigeminal nerve group and that the muscles they supply arise differently to those supplied by the trigeminal, belonging according to my nomenclature to the somatic group of muscles, and not to the splanchnic group. These eye muscles are remarkably constant throughout the vertebrate kingdom, and are as well defined i Petromyzon as in the higher vertebrates; although the may be said to belong, to the somatic group of muscles, by no means follows that they arose as part and parcel the great longitudinal muscle sheet from which the som muscles of the body have arisen. The study of the musc system in Ammocœtes shows that the striated muscl the animal fall into three categories, (1) the longitu somatic muscles which are distinguished most marke their structure, their origin, and their innervation; (

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[1] N.B.—In the figure the velar branch of the trigeminal V_3 is though it went to the most ventral tentacle. This is wrong, it reall the lower lip

visceral or splanchnic muscles; and (3) the eye muscles; these latter resemble the visceral group in structure, but arise from v. Wijhe's foremost dorsal mesoblastic segments, which he ranks as continuous with the trunk somatic segments and not from the ventral splanchnic mesoblastic segments. In addition, these eye muscles do not in direction belong to the longitudinal group, but may be spoken of as forming a dorso-ventral rather than a longitudinal group of muscles. Confusion has to my mind arisen in endeavouring to force the somatic eye muscle group into the same group as the longitudinal somatic muscles. It seems to me highly probable that a solution is more likely to be found if these muscles are considered in a separate group—somatic if you like, but not belonging to the spinal longitudinal muscles. The solution which I offer tentatively is as follows:—As already mentioned, the prosomatic segmental nerves in Limulus and the Scorpions, just like the mesosomatic are made up of three nerves, the dorsal or epimeral nerve being sensory for the supply of the prosomatic carapace, the middle or lateral nerve being mixed for the supply of the prosomatic appendages, and the ventral nerve being mixed, in all probability, for the supply of the somatic muscles of the prosoma. Of these three nerves the descendants of the first two groups are represented by the trigeminal nerves, both motor and sensory, just as the descendants of the same two groups are represented in the mesosomatic region by the ascending root of the trigeminal and the facial, glosso-
haryngeal and vagus nerves. Hitherto the third set of
erves has not been considered either in the mesosomatic or
osomatic region. The history of the nerves which on my
w correspond to this third group is given by v. Wijhe's
estigations; in his scheme the first and second dorsal
ites give origin to the muscles innervated by the oculo-
r and trochlearis nerves respectively, the corresponding
al segments being innervated by the trigeminal; the
dorsal somite gives origin to the muscles innervated
abducens, and the corresponding ventral segment
to the facial nerve; the corresponding dorsal

somites of the fourth, fifth and sixth segments belonging, according to him, to the facial, glosso-pharyngeal and vagus groups do not develop any muscles. Next come the longitudinal muscles innervated by the hypoglossus, muscles which are recognised now-a-days as innervated by the spino-occipital nerves, and thus form the foremost of the spinal longitudinal group of muscles. My interpretation of v. Wijhe's facts would be that the eye muscles alone represent all that is left of the somatic muscles of the prosomatic and mesosomatic segments, and that v. Wijhe's evidence goes to show that whereas these muscles of the prosoma are represented by the oculomotor and trochlearis group, the corresponding muscles of the mesosoma have been lost, with the exception of the external rectus innervated by the abducens.

The description of the muscular system of Limulus and Scorpion has been well given by two pupils of Ray Lankester, Benham and Miss Beck.[1] In both cases the muscles are divisible into three groups, viz.: the muscles of the appendages and two groups of muscles of the soma, viz., a longitudinal group and a dorso-ventral group. Most characteristic are the mesosomatic dorso-ventral muscles in both animals, the vertical mesosomatic muscles as Benham calls them. In each paired segment a pair of these muscles passes from the sternal to the tergal surface; in the prosomatic region these segmental dorso-ventral muscles still continue, but are not so simply definable in this region owing to a greater concentration of the muscles in this region and to the presence of the plastron. We may, however, fairly say that a segmentally arranged series of dorso-ventral somatic muscles are
marked characteristic of the prosomatic and mesosomat
regions in both Limulus and Scorpions.

I suggest then that the reason for the peculiarities of t
eye muscle group, the reason why they must be placed i
separate category to all other muscles, is given if the do
ventral segmental muscles of the prosomatic regio
represented by the muscles innervated by the oculomoto
trochlearis nerves, while the corresponding muscles

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[1] *Trans. Zool. Soc.*, vol. xi., 1885.

mesosoma have disappeared with the exception of the external rectus innervated by the abducens.

If this be so, then the oculomotor and trochlearis nerves ought to correspond to the same number of segments as the motor trigeminal nerves, and conversely if reason be given that the oculomotor nerve is not a single segmental nerve, but supplies many segments, then the number of segments supplied by the oculomotor and trochlearis ought to help the determination of the number of segments belonging to the motor part of the fifth. It seems clear that no sufficient evidence has been given morphologically which compels us to look upon the oculomotor nerve as a single nerve. Rabl[1] has pointed out that v. Wijhe's most anterior segments look more like an amalgamated series of segments than separate segments, comparable to those in the spinal region, and it is clear that if, as I have urged, this region is characterised by a special concentration, that that concentration may have affected the formation of the peripheral segments as well as the nervous metamers.

To turn from the embryological evidence to the anatomical, the teaching of recent anatomy is distinctly in favour of a multiple origin of the oculomotor nerve; we see that the observations of Perlia on new-born animals led him to the conclusion that the nucleus of origin of the oculomotor nerve is made up of a number of cell groups quite distinct from each other, each group being comparable to the nucleus of the trochlearis. The older observations of Hensen and Völkers were to the effect that the terminal branches of the oculomotorius, *i.e.*, the nerves to the separate eye muscles, are arranged sagitally behind each other, and can be separated physiologically. Bernheimer, Schwabe and ach have recently by the degeneration method endeavoured settle which muscles are innervated from the nucleus of opposite side, and what are the limits of the nucleus of nerve of each muscle. Further observation is necessary re we can speak with certainty on this point, but enough been done to lead distinctly to the conclusion that the us of origin of the oculomotor nerve is composed of a

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[1] *Anat. Anzeige*, 1892, p. 104.

series of nuclei, each of which is equal in value to the nucleus of the trochlearis. Each of these gives origin apparently to one of the nerves belonging to one of the eye muscles. Some of these cross like the trochlearis to supply the muscles of the opposite side, while some pass direct to the muscles of the same side. If then each superior oblique muscle represents a dorso-ventral somatic muscle of a segment, similarly each inferior oblique, superior rectus, inferior rectus and internal rectus represents the corresponding dorso-ventral muscle of four other segments, and I should come therefore to the conclusion that the oculomotor and trochlearis nerves represented the ventral somatic nerves of at least the first five prosomatic segments, the appendages of which are represented by the upper lip and tentacles. I say at least because the meaning of the levator palpebræ superioris and the retractor bulbi muscles has not been considered. Coming now to the abducens and the external rectus muscle I cannot agree with Hatscheck[1] that this muscle arose in Ammocœtes as part of the longitudinal system of somatic muscles; it belongs to the dorso-ventral group just as much as the other eye muscles, and has the same structure. Its nucleus of origin belongs rather to the facial region than to the trigeminal, and the muscle arises according to v. Wijhe in connection with the facial segment. Neal[2] has published lately an interesting account of the relation of the abducens to the neuromeres, from which he concludes that the abducens is the sole representative of a series of ventral nerves belonging to the facial, glosso-pharyngeal and vagus segments. These nerves in all probability originally innervated opisthotic musculature; the muscle of one, however has taken up a prootic position, and this one alone ha survived in the shape of the external rectus.

Translating these conclusions of Neal into the langua of this paper, I should say that the external rectus mu is the sole survivor of a series of similar dorso-ventral m somatic muscles, and that it has survived because it taken on a prosomatic position in connection with the other prosomatic dorso-ventral muscles.

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[1] *Anat. Anseiger*, 1892.

[2] Neal. "The segmentation of the nervous system in *Squalus aca* *Bull. of Mus. of Comp. Zool.*, Harvard, vol. xxxi., p. 147, 1898.

An additional plausibility is given to this suggestion by the observation of Benham that the dorso-ventral somatic muscle of the foremost mesosomatic segment in Limulus has taken up a prosomatic position, owing to the shifting of the foremost entapophysis on to the prosomatic carapace.

I suggest, then, that the eye muscle-nerves may very well be the remnants of the nerves which supplied the dorso-ventral somatic muscles of the prosoma; the abducens alone having originally belonged to the mesosomatic region. Such an explanation gives an adequate reason for the absence of muscle spindles in these muscles, as noticed by Sherrington, an absence which would be decidedly improbable if these muscles were originally part of the ordinary somatic muscles of the body. It also to my mind explains Sherrington's inability to find the ganglia cells of the sensory nerves of these muscles, for if they are the only remnant of this old somatic muscular system, I should expect that the cells of their sensory nerves would be in the oculo-motor nucleus itself, or, at all events, within the brain, and not yet differentiated into posterior root ganglia.

GIANT-CELLS AND GIANT-FIBRES.

This trigeminal or prootic region of the brain affords yet another clue, which I cannot help thinking is of great significance, viz., the presence and function of the giant-cells and giant-fibres.

These fibres are the well-known Mauthnerian fibres of
e fish, which arise from the giant-cells in the region of
e eighth nerve. These giant-cells, one on each side, are
st conspicuous on each side of the middle line, and send
r dendritic processes to mingle with the fibres of the
h nerve, their axis-cylinder process, which forms the
hner fibre, crosses soon after it leaves the cell, and
down the cord right to the tail; here it breaks up,
believed by Fritsch[1] and others to supply directly the

Fritsch. *Untersuch. üb. d. feineren Bau d. Fischgehirns*, Berlin, muscles of the tail. Thus Bela Haller[1] says:—"The Mauthnerian fibres are known to give origin to certain fibres which supply the ventral roots of the last three spinal nerves; so that their end branches serve in all probability for the innervation of the muscles of the tail fin." They do not occur, according to Haller, in the eel, or in the Siluroids, according to Kolliker.[2] For this reason Fritsch's original conclusion that these giant-fibres are associated axis-cylinders for certain definite coordinated movements of the fish, especially for the lateral movement of the tail, gains in probability. When we pass to the Ammocœtes we find this system of giant-fibres, which are here called Müllerian fibres, more extensively represented. The giant-cells are divisible into three groups. The first group consists of three pairs in front of the fifth nerve, of which two are in front of the exit of the third nerve and one pair at the origin of the third nerve.

The second group consists of a number of cells in the region of the nucleus of the fifth nerve.

The third group consists of a number of cells at the level of the entrance of the fibres of the eighth nerve.

The largest cells are found in the first and third groups. The Müllerian fibres, to which these cells give origin, largely decussate, as described by Ahlborn, and then become the most anterior portion of the white matter of the cord, forming a group of about eight fibres on each side. A few fibres are also found laterally and slightly dorsally to the grey matter. These giant-fibres pass down the cord righ to the anal region; their ultimate destination is unknow Mayer[3] considers them in the first part of their course form the posterior longitudinal bundle, and I should imagi therefore, that the spinal part of their course would rep sent the antero-lateral descending tract, and that the t group in connection with the eighth nerve represents Dei nucleus; the whole system being probably a coordin mechanism, connected possibly with the maintena muscular tone, which arises entirely in the prootic or prosomatic region of the brain, the great coordinating and equilibration region *par excellence*.

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[1] *Morphol. Jahrbuch*, vol. xxiii., 1895, p. 98.
[2] *Handbuch der Gewebe Lehre*, 6 Aufl., vol. ii., 1893, p. 169
[3] *Anat. Anzeig.*, bd. xiii., p. 649.

If we turn now to the Arthropod, it is a striking coincidence that in the crayfish and in the lobster the work of Retzius,[1] of Celesia,[2] of Allen,[3] and many others, demonstrate that an equilibration mechanism exists for the swimming movements of the tail muscles, which is carried out by means of giant-fibres, which run as axis-cylinder processes of giant-cells in the brain region through the whole ganglion chain, to supply the tail muscles; nay, more; just as the Mauthnerian fibres are said to branch and supply the tail muscles with motor fibres directly, so the two giant fibres in the crayfish cord, according to Retzius, branch at the last abdominal ganglion, to pass out directly with the nerves to the tail fin. Allen has shown that in addition to these two giant-fibres, there are a number of other fibres, some of which cross, some do not; each of which arises from a large nerve-cell and passes to the last abdominal ganglion. These latter fibres, he says, send off collaterals, while the two giant-fibres do not. The cells which give origin to all these large, long fibres are situated in or above the prosomatic region of the brain, just as the giant-cells, which give rise to the corresponding Müllerian fibres of Ammocœtes. How far this system is represented in Limulus or the Scorpion I do not know.

It is to my mind improbable that the Mauthnerian fibres should pass out directly as motor fibres to the muscles of the
ail fin; it is more likely that they are conducting paths
etween the equilibration mechanism in connection with the
hth nerve and the spinal centres for the movements of the
l. Similarly with respect to the arthropod it is difficult
believe that the motor fibres for the tail muscles should
e in the brain region. In either case, the striking coinci-

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iol. Untersuch., i. 1890. "Zur Kenntniss des Nervensystem der
een."

*ferensiamento d. proprietà inhib. e. d. funsioni coordinatrici n. catena
e d. crostacei decapodi*, Genoa, 1897, p. 80.

udies on the Nervous System of Crustacea," *Q. J. of Micr. Sci.*, vol.
461.

dence remains that the movements of the tail end of the body are regulated by means of giant-fibres which arise from giant-cells in the head region of the body in both the arthropoda and the lowest members of the vertebrata.

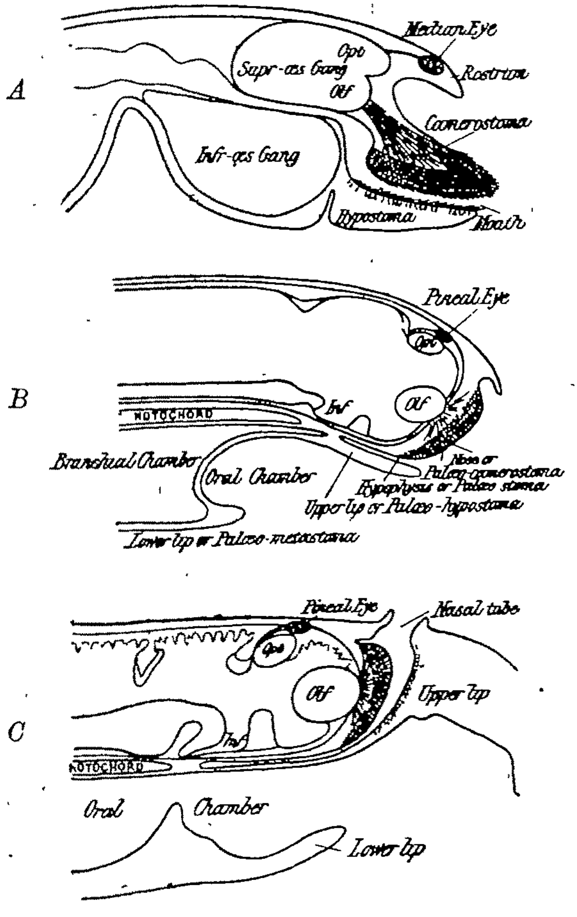

FIG. 18.

A, median sagittal section through head of young Thelyphonus; *B*, m
sagittal section through head of young Ammocœtes; *C*, median sagittal s
through head of full grown Ammocœtes.

In order to complete this history of the meaning
cranial nerves, I ought now to consider the nerves of
sense, especially the auditory and olfactory. It is, h
impossible in the limits of a single address to bring

you all the coincidences which exist between the cranial nerves of Ammocœtes and the nerves of the Scorpion and Limulus group. I will content myself with mentioning that, as pointed out in my address to the British Association at Liverpool, the auditory nerve and auditory capsule may well be represented by that extraordinary sense organ—the flabellum—of Limulus, while the olfactory nerve and nasal organ of Ammocœtes, as is seen in fig. 18, corresponds most closely with the camerostome of the Scorpions, Thelyphonus, &c.

The views which I have put before you can be presented in the form of the following table, which is intended only to represent the general nature of my conclusions, and in the last column I give v. Wijhe's segments to show how they compare with mine.

Such then is the conclusion to which my theory of the origin of the central nervous system of vertebrates from the central nervous system of an arthropod ancestor logically leads, viz., that the cranial segmental nerves represent the original type of segmental nerves, and are all derived from the corresponding segmental nerves of the arthropod. The spinal type is a more recent type, and like the spinal cord is a vertebrate characteristic. One great reason why I feel that my theory is based on true lines, and will ultimately be accepted, is because it is in harmony with what is to my mind the great
ading conception underlying the whole evolutionary pro-
ss, that all upward progress in the animal world is corre-
ed with a steady growth of the central nervous system,
ecially of the foremost part of it or brain.

Table of comparison of corresponding segments and appendages in the Arthropoda and Vertebrata.

		Segments.	Astacus.	Limulus.	Scorpio.	Thelyphonus.	Ammocœtes.	Nerves to Appendages.	Nerves to dorso-ventral muscles of somatic segments.		v. Wijhe's segments.
Supra-œsophageal.			Lateral eyes Antennules	Median eyes Lateral eyes	Median eyes Lateral eyes Camerostome	Median eyes Lateral eyes Camerostome	Pineal eyes Lateral eyes Olfactory organ	Pineal II I			
Infra-œsophageal.	Prosomatic.	1	Antennæ	Chelicerae	Chelicerae	Chelicerae	1st Tentacles (?)	V_1			
		2	Mandibles	1st Locomotor	Chelæ	Pedipalps	2nd "	V_2	III_1	Eye muscles supplied by oculomotor nerve	
		3	1st Maxillæ	2nd "	2nd Locomotor	2nd Locomotor	3rd "	V_3	III_2		1
		4	2nd "	3rd "	3rd "	3rd "	4th "	V_4	III_3		
		5	1st Maxillipeds	4th "	4th "	4th "	5th "	V_5	III_4		
		6	2nd "	5th "	5th "	5th "	6th "	V_6	III_5		
		7	3rd "	Chilaria	Missing in adult Present in embyro	Metastoma in Eurypterus	Velum and lower lip	V_7	IV	Sup. Oblique	2
	ic.	8	1st Ambulatory	Opercular	Opercular	Opercular { Genital	Thyroid	VII_1	VI	Ext. rectus	3
		9	2nd "	1st Branchial	1st Branchial	1st Branchial	Hyoid or 1st Branchial	VII_2	lost	lost	4
		10	3rd "	2nd "	2nd "	2nd Branchial	2nd Branchial	IX	lost	lost	5
			4th "	3rd "	3rd "		3rd "	X_1	lost	lost	6
				4th "	4th "		4th "	X_2			7
				5th "			5th "	X_3			8
							6th "	X_4			9
							7th "	X_5			

CEREBRAL DIPLEGIA.

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THE subject matter of this paper consists of three parts :—

Part I.—An account of some cases of cerebral diplegia from the wards of the National Hospital, with a pathological report upon two cases by Dr. Risien Russell.

Part II.—A summary of the present knowledge and opinions concerning cerebral diplegia.

Part III.—A bibliography of the subject.

PART I.

An Account of some Cases of Cerebral Diplegia observed at the National Hospital.

The following cases of typical cerebral diplegia show important ætiological relations and a progressive and inter- sting symptomatology.

In the literature of the subject there are very few cases corded in which there has been an opportunity for patho- gical investigation of the central nervous system, at a time en the onset of the disease was still comparatively recent. ch difficulty has arisen in the attempt to correctly esti- the nature of the initial morbid process of the disease the anatomical characters of central nervous organs ned at a time relatively remote from the onset of the during which time secondary morbid processes, sclerosis, tissue absorption, &c., have occurred. In he cases the central nervous system was examined nost recent methods of histological investigation er the onset of the malady, death having occurred while the symptoms were still progressing, and while it may be fairly argued that the initial morbid process was still active. In these cases the same pathological condition was found, and it throws considerable light upon the origin of diffuse and lobar cerebral sclerosis, which are commonly the final lesions found in cases of cerebral diplegia.

I am indebted to the kindness of Dr. Bastian, Sir William Gowers, Dr. Ormerod, and Dr. Tooth, for permission to publish the notes of these cases, and to Dr. Risien Russell for the pathological report.

Case 1. *Generalised Rigidity: Autopsy.*

H. G., aged three years, was admitted into the National Hospital under the care of Dr. Bastian in December, 1897, with paralysis and rigidity of all four limbs and inability to speak.

The family history was unimportant. The father denied venereal disease, and no facts were elicited suggesting syphilis. The patient was the youngest but one of five children, and the other four were strong and well.

The history was as follows:—

She was a full term child, and the birth was natural. She began to talk and walk at eighteen months old, but she was never able to walk alone. At this time she was much frightened by a lamp explosion in the room where she was sleeping, and the mother stated that she had been very nervous ever since. She had none of the usual ailments of childhood.

In August, 1897, she appeared to be generally unwell, and di
not take her food for a few days. She was very fretful, and
was noticed that she began to have difficulty in crawling abou
She gradually became weaker in the limbs, and the limbs becam
stiff. She gradually lost her speech, and in November, 1897, s
began to have great difficulty in swallowing, and the legs bec
"stretched out stiff" and could not be bent. She had no f
convulsion at any time.

On examination she was a poorly nourished, fresh comple
child, with no signs of congenital syphilis. As she lay in h
appearance was very remarkable. There was spontaneo
nystagmus of small range, both rotatory and lateral.
wore a fixed, rather bright expression, with the eyes w
and staring. There was absolutely no emotional pl
features, and when she cried the angles of the mouth w

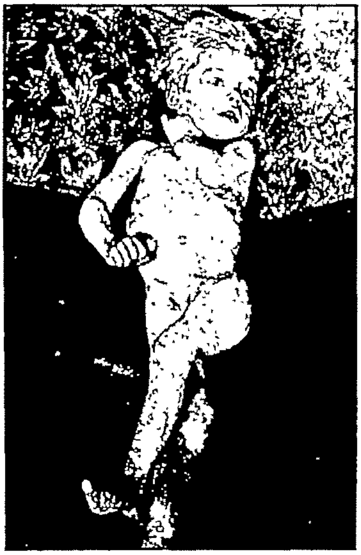

FIG. 1.

Attitude in Generalised Rigidity. Case 1.

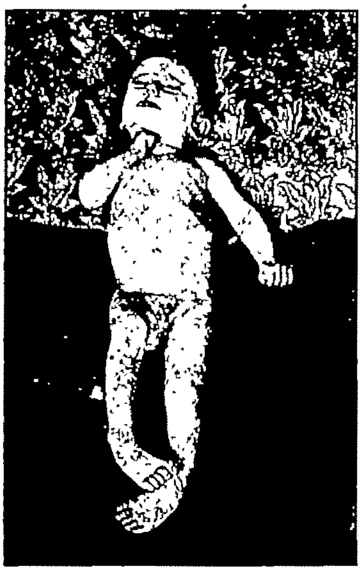

FIG. 2.

Attitude in Generalised Rigidity. Case 2.

drawn back to a slight extent; the expression was "starched"; the head was slightly retracted.

The left arm was held across the chest, rigidly flexed to an acute angle, the right was less rigidly extended by her side.

Both lower extremities were rigid, and there was pes cavus in both feet. The right knee was hyperextended to a marked degree; the right foot was dropped.

The left knee was kept rigidly flexed at an angle of 120°, and was adducted so as to cross the other knee. The abdomen was retracted.

This facial aspect and the position of the limbs did not change at all during the nine months she remained in hospital.

Her mental state was very much reduced. She would turn her head when her name was called, and would follow a bright object with her eyes. She tried to laugh when a doll was given her. She uttered no articulate sound at all. She did not seem to understand simple questions.

Vision did not seem to be much impaired, but both optic discs were very pale and atrophic, and the vessels were small. There was no deafness. The pupils were equal and reacted normally. There was marked spontaneous rotatory and lateral nystagmus. The ocular movements otherwise were good, and there was no strabismus.

The palpebral fissures were wider than normal, and the face wore the curious fixed expression described above. When the child screamed the lower face was more drawn down on the left side than on the right.

There was great difficulty in swallowing; only small quantities of semi-liquid food could be taken without the patient choking.

All the trunk muscles were stiff, and respiration was preonderatingly abdominal.

The position and rigidity of the limbs has been already deribed. She could make all the movements of the left arm wly and clumsily, but she was entirely unable to move the ht arm and both legs.

There was great pain on any attempt at passive flexion of the l joints.

ensation seemed quite unaffected. The sphincters acted rally.

The plantar reflexes were brisk, and were of the extensor type. The abdominal reflexes were brisk. The knee-jerks were present, but very difficult to obtain on account of the rigidity. No foot clonus was obtained.

The child remained in the same condition, except that the left arm gradually became rigid and motionless, and that there was considerable emaciation. An attack of broncho-pneumonia proved fatal in September, 1898, ten months after admission.

Fig. 1 is taken from a photograph of the patient four months after admission.

In the history of this case there is nothing to suggest the cause of the disease. The child began to walk at the usual age, and though apparently healthy till two years and nine months old, was never able to walk alone. This fact suggests that some pathological process was in operation long before the onset of definite symptoms. The mother's account of a fright may probably be dismissed as an instance of the tendency to attribute illness to some definite incident which has become fixed in the memory of the person from whom the history of an illness is obtained. It is likely that the general ill-health immediately preceding the onset of definite symptoms may have been an important factor in the precipitation of a morbid process already in activity, rather than the initial manifestation of disease in a healthy subject. That these symptoms were evidence of an acute tissue process causing the disease is, I think, rendered unlikely by the subsequent regularly progressive course of the disease, when the general health of the patient appeared normal. It is especially important, in the consideration of cerebral diplegia, to bear in mind that the sudden appearance of symptoms in an apparently healthy subject does not argue against the congenital origin of the disease. The tissues are endowed with a certain tenure of life only, and their tenure of lif may be greatly shortened by the occurrence of morbid pr cesses during development and by hereditary influenc Congenital morbid processes may suddenly produce sym toms in subjects who have been apparently healthy fo long period. The truth of this assertion is frequently denced in cases of hereditary insanity, adolescent ge paralysis, Friedrich's disease, myopathy, &c. The effe an acute illness in precipitating symptoms due to an alrea acting morbid process is, perhaps, often not sufficiently recognised, and what is in reality only an immediate exciting cause is considered the ultimate factor in disease. The not uncommon occurrence of the first symptoms of tabes, disseminated sclerosis, and paralysis agitans, after attacks of influenza, serves as a good example of the immediate exciting effect of acute illness upon chronic morbid processes.

The clinical picture of the case was one of severe generalised rigidity. Some of the signs are worthy of comment. Optic atrophy is of rare occurrence in these cases, and has been reported only in the more severe forms of this disease. It is probably due to the same pathological process affecting the retina as occurs in the cerebral cortex. The spontaneous nystagmus, staring expression and mask-like face are cardinal signs of spasticity of the ocular and facial muscles.

Difficulty of deglutition occurs not infrequently, and is referable to slow contraction and stiffness of the pharyngeal muscles. Head retraction, which may be sufficiently marked to suggest the presence of meningitis, occurs in cases where the trunk is severely affected. The extensors of the neck are much stronger muscles than the flexors, and when both flexors and extensors are equally rigid, a position of extension of the head occurs.

The position of the limbs in this case, and in the next to be described, was peculiar, combining two characteristic attitudes described in cerebral diplegia; the left limbs being in the "attitude of adoration," and the right limbs in a position of rigid extension (*vide infra*).

Where voluntary movement was possible the preponderance of rigidity over loss of power was marked. This preponderance of rigidity over paralysis is characteristic of cerebral diplegia.

Pathological Report by Dr. Risien Russell.

An autopsy was performed twenty hours after death.

The dura mater was slightly adherent in places to the arachnoid over the upper part of the convexity of the hemispheres.

The lepto-meninges were irregularly thickened over the upper part of the convexity of both hemispheres, the process being evidently chronic, and no evidence of fresh exudation or pus was detected.

There was well-marked compensatory œdema of the pia arachnoid.

The convolutions of both cerebral hemispheres showed marked general atrophy, with widening of the sulci, the condition being most pronounced in the frontal lobes and upper part of the central convolutions, but the occipital lobes also presented somewhat of a "rabbit's intestine" appearance.

On palpation the brain felt unduly firm, and there was nothing in its appearance or to the touch which suggested the presence of hydrocephalus. The meninges at the base showed absolutely no sign of thickening or other evidence of old or recent meningitis, and they were equally free from any such change at the exit from the fourth ventricle.

After the brain had been hardened in formalin, sections into each cerebral hemisphere at different levels failed to reveal any abnormality in connection with the centrum ovale, internal capsule, basal ganglia or any other part.

When the lepto-meninges were removed a general granular appearance of the cortex was obvious. The condition, as seen on macroscopical examination, suggested a sclerosis of the cortex with shrinking.

The lungs showed marked broncho-pneumonia.

Parts of the central nervous system were preserved in formalin, and other parts in Müller's fluid, and in the subsequent examination of sections made from the brain, cerebellum, pons, medulla, spinal cord, and optic nerves, the methods of staining employed included those introduced by Nissl, Marchi, and Pal, in addition to which stains such as hæmatoxylin, eosin, and aniline blue-black were used.

Brain.—Apart from the patchy thickening of the meninges already described, no evidence of meningitis is seen, nor is there any undue engorgement of the meningeal vessels, whose walls further appear free from any abnormal thickening. The cerebral substance itself is equally free from any inflammatory changes, either of an acute or chronic character. The blood-vessels are not unduly plentiful, they are not engorged, their walls are natural, and none of them are seen to be thrombosed. Moreover, there is no sign of any perivascular round cell proliferation, no hæmorrhages, and no increase of interstitial tissue that can be regarded as constituting any sclerosis of the brain. The feature which arrests the attention of the observer on examination of sections from different regions of the cortex of both cerebral hemispheres is the great paucity of pyramidal cells. In some parts scarcely a cell of the kind is revealed by the stains employed, while in other parts groups of pyramidal cells are seen; but even these are obviously greatly altered, most of them presenting a marked degree of atrophy. There is nothing in the appearance of the cells to suggest anything of the nature of an acute degeneration, for neither the cells nor their nuclei present any signs of swelling, nor is destruction of the cells with extrusion of their nuclei a feature in the changes seen. Many of the cells present preserve more or less of their normal pyramidal shape, but they are all below the normal in size, many of them very much so. There is a diffuse staining of the cells by the Nissl method, with no tendency to picking out of the so-called Nissl bodies or chromatic substance which forms so striking a feature in normal pyramidal cells treated according to this method.

Pons and medulla.—Apart from degeneration of the pyramidal fibres on both sides of the pons and medulla, there is no obvious change either of the nature of a secondary degeneration or sclerosis of any of the other tracts of fibres such as the fillet, posterior longitudinal bundles, superior and inferior cerebellar peduncles, and the like, or of the nature of an inflammatory reaction, or a softening the result of thrombosis. With regard to the degeneration of the pyramidal fibres, it is noteworthy that in sections prepared by the Marchi method but few nerve fibres show the typical reaction to osmic acid which we are in the habit of meeting with when there is acute destruction of the myelin sheaths. The myelin sheaths of a large number of the fibres stain rather a greyish black instead of the usual intense black colour, and there is in addition a diffuse speckling of the section with black dots within the degenerated areas. The appearances which are being described are not due to *post-mortem* change; but from the experience which I have gained from similar observation in other cases, I am led to regard them as evidence of nutritional changes occurring slowly in the myelin sheaths as opposed to the rapid changes which occur when they are suddenly severed from their source of tropic supply. In short, the changes presented by the myelin sheaths of the pyramidal fibres are compatible with some slowly progressing degenerative or atrophic change going on in the part of the neuron known as the cell, rather than with any acute destruction of the cells.

As seen with the unaided eye in sections stained by Pal's method, the pyramids appear completely degenerated, but under the microscope many nerve fibres are seen to be normal, these being of various sizes; more of these are present in one pyramid than in the other. Many pyramidal fibres that still stain when sections are treated by Pal's method are swollen and obviously changed to a variable degree.

Spinal Cord.—There is marked degeneration of the crossed and direct pyramidal tracts on both sides of the cervical region of the spinal cord, the area occupied by the degeneration, in regard to both the crossed and direct pyramidal tracts, being more extensive on one and the same side of the cord than on the opposite side. The same distribution of the degeneration is met with in sections taken from different levels throughout the whole extent of the thoracic portion of the cord; but whereas the degeneration of the crossed pyramidal tracts is still distinct throughout the lumbar and even in the sacral region, no obvious degeneration is seen in the direct pyramidal tracts, with the unaided eye, in sections prepared by Pal's method. Under the microscope, however, the degeneration of the direct pyramidal tracts can be traced into the lumbar region of the cord; this is an especially easy task in so far as the more extensively degenerated direct tract is concerned. In the sacral region, however, no definite indication of degeneration of either direct tract can be determined.

All the other tracts of the spinal cord are natural, none of them presenting any evidences of degeneration or other change, while the grey matter is everywhere equally free from any obvious abnormality.

Optic Nerves.—As seen both on longitudinal and transverse section, there is obvious atrophy and degeneration of the optic nerves. The bundles of nerve-fibres are shrunken, and the spaces between them much in excess of the normal, but there is nowhere any evidence of inflammatory changes occurring in the interstitial tissue.

Case 2.—Generalised Rigidity : Autopsy.

D. J., aged 2½ years, was admitted into the National Hospital, under the care of Dr. Bastian, on April 18, 1898. Her mother said that she had lost the use in all her limbs since a fall three months before.

Both parents were healthy, and the father denied venereal disease. One child of their family was alive and well, and one died, prematurely born.

The mother's last pregnancy was a molar pregnancy. There was no history of nervous disease in the family.

The history of the case was as follows:—

The patient was born at full term, and the birth was natural. She was quite healthy till the onset of this illness, three months before admission. She was always a bright, intelligent child, and could walk well when the illness came upon her. She had not learned to talk.

Three months before admission, when in perfect health, she had a fall against the edge of a tub, but did not strike her head, and did not seem to be much hurt. To this fall the mother attributed the illness.

Three days later she was noticed to be poorly, and did not take her food. On the following day she complained of her head aching, and she was noticed to squint and to be unsteady on her legs. After this all four limbs gradually became weak, so that the child could not sit up, and a month afterwards all four limbs had become stiff, and had assumed the position to be subsequently described.

The headache was only complained of for two days. The child had not been convulsed, nor had she vomited at any period of her illness.

A fortnight before admission the mother first noticed difficulty in swallowing, and that the head was thrown back.

On examination the patient was a well-nourished, delicate-looking child. She lay on her back in bed, with the head slightly retracted. She was very fretful, and quite conscious. She put out her tongue and grasped a finger on command. She did not utter any articulate sound.

So far as they could be tested, the special senses seemed normal. Vision was certainly acute. The optic discs were normal.

The pupils were unequal; right = 5 mm., left = 2·5 mm. Both reacted to light, and during convergence, but the right much more sluggishly than the left.

There was quick, spontaneous rotatory and lateral nystagmus, of small range, in all positions of the optic axes.

There was no strabismus, and the ocular movements were good. She followed a bright light presented to her view, perfectly in every direction.

The face had a fixed, starched, pained expression, and there was a marked absence of any emotional play of the features. This was particularly noticeable when the child was crying. There was considerable difficulty with deglutition, and it was necessary to feed her with semi-solid food.

There was marked rigidity in all the trunk muscles. Respiratory movements were preponderatingly abdominal.

The condition and position of the limbs closely resembled those of the patient H. G. They presented no marked wasting and no tremor. The elbows were rigidly flexed to an acute angle, and adducted (attitude of adoration). She did not move the elbow or shoulder joints at all. Passive movements at these joints required much force, on account of the extreme rigidity, and such movements caused great pain. She could flex and extend the fingers imperfectly and slowly. The left lower limb was rigidly extended, and the left knee was hyperextended. The right lower limb was rigid, in a position of slight flexion and adduction at the hip joint, and flexion at the knee joint.

Both feet were dropped, the dorsa being in a line with the tibiæ, and were inverted. She could move the lower extremities at all joints, but very feebly, and with a very small range of movement. The rigidity of the lower extremities at all joints was so great that extensive passive movements were impossible, and the attempt to perform them produced great pain.

So far as could be ascertained, there was no defect of objective sensation, and she did not appear to suffer any pain except when the limbs were moved.

The sphincters were normal. The cranium was normal, except that the anterior fontenelle was still to be felt.

The plantar reflexes were present, and showed an extensor response on both sides. The abdominal reflexes were brisk. The knee-jerks were obtained with difficulty, owing to the rigidity. No ankle clonus was obtained. This patient remained in the hospital until her death six months after admission. She emaciated considerably, and had several attacks of broncho-pneumonia, the last of which proved fatal. During this time the aspect of the case did not alter materially. Swallowing became more difficult, and the four extremities became completely paralysed and rigid. The position of the upper extremities changed. The left arm became rigidly extended a month after admission, and at this time a photograph, reproduced in fig. 2, was taken.

Subsequently the right arm became extended, and both arms became adducted to the sides and pronated to an extreme degree, so that the olecranon processes looked directly forwards (extension pronation attitude). The condition of the lower limbs, the nystagmus, the inequality of the pupils, and the optic discs remained the same.

In this case there are some facts suggesting a pathological maternal condition during pregnancy. The child preceding this one was prematurely born, and lived only a short time, and the pregnancy following the birth of this patient was a molar pregnancy.

As in the first case reported here symptoms of general illness immediately preceded the onset of the nervous symptoms, and up to this time nothing had suggested that the child was not absolutely healthy.

The clinical picture was almost identical with that of the preceding case. The transient squint, inequality of the pupils and slowness of pupil reaction have been noted in many recorded cases.

Pathological Report by Dr. Risien Russell.

The autopsy was performed fifteen hours after death.

The skull cap and dura mater were natural. The brain was considerably smaller than the bony case of the skull, there being a large space between the inner surface of the bone and the surface of the cerebrum. The lepto-meninges were natural, and there was no evidence of meningitis. Although the brain was obviously small as a whole, there was very little shrinking of the convolutions or widening of the sulci; but the latter were a little more marked than normal about the central convolutions and hinder part of the frontal lobe.

The arrangement of the convolutions was normal, and there was none of the "rabbit's intestine" appearance of the frontal and occipital lobes such as was seen in the case of H. G. There was no softening of the convolutions on the surface and no evidence of hydrocephalus. On palpation the brain was unduly firm. The pia mater could be stripped from the convolutions without tearing the cortex. The cerebellum, pons and medulla appeared normal. After hardening in formalin the surface of the convolutions presented a granular appearance when the pia arachnoid was stripped off such as was seen in the case of H. G., but to a much slighter extent.

On making horizontal sections into the two hemispheres no gross change was found. The grey matter was obviously reduced in places, though more or less irregularly so. The white matter was also reduced, quite narrow bands representing the internal capsule and the entering fibres from the frontal and occipital lobes. The basal ganglia, on the other hand, appeared well developed.

As in the case already described, so in this one, parts of the central nervous system were preserved in formalin and other parts in Müller's fluid, and the stains employed in the preparation of sections for microscopical examination were those devised by Nissl, Marchi, and Pal respectively, in addition to which hæmatoxylin, eosin, and aniline blue-black were used.

Brain.—Microscopical examination of the cerebral meninges reveals evident œdema of the pia arachnoid, the two layers of the membrane being separated from each other to a considerable extent without there being anywhere the slightest evidence of any inflammatory reaction. The vessels of the meninges are natural, and there is no perivascular proliferation of round cells, no multiplication of nuclei, and the like; and apart from the spacing out of the meninges in consequence of the œdema, there is no evidence of thickening of them indicating any past or chronic inflammatory change. Nowhere is there any sign of unduly thickened bands of fibrous tissue extending into the substance of the cerebral cortex from the pia mater.

The great feature which immediately obtrudes itself on the observer on microscopical examination of the cortex is the singular scarcity of pyramidal cells. This remark applies to all the different layers of these cells. Not only is there a great paucity of such cells, but those that are present are obviously markedly changed. Scarcely a pyramidal cell is to be seen which reaches the normal standard as regards size; the majority of them are considerably atrophied and shrunken, but none show any evidence of swelling of the cell or of its nucleus, nor is there any evidence of destruction of the protoplasm of the cells with extrusion of their nuclei and so on. There is a diffuse staining of the chromatic substance of the cells instead of the so-called Nissl bodies being picked out as obtains under normal conditions. The change is patchy in distribution, for while in parts scarcely a pyramidal cell is revealed by the stain, in other parts groups of such cells are seen, some of which are extremely atrophied, while others preserve more or less of their normal pyramidal shape. These changes do not appear to be limited to any one region of the cerebral cortex, as though sections were examined from different parts of both cerebral hemispheres, in all the same changes were seen, evidently consisting in a primary degeneration of the neurons of the cortex. Whether any of the paucity of the pyramidal cells is due to their never having developed, or whether all the changes are to be ascribed to degeneration of such cells which had at one time been normally developed, it is not, of course, possible to say.

The blood-vessels in the cortex are not unusually plentiful, they are not engorged, and their walls show no evidence of any undue thickening.

There is nowhere the slightest sign of any inflammatory reaction, such as perivascular round-cell proliferation, multiplication of nuclei, and the like. Nor is there the slightest sign of sclerosis, as evidenced by increase of interstitial tissue. Moreover, no thrombosed vessels and consequent softening of cerebral substance is anywhere to be seen.

The cerebellum, pons, and medulla oblongata also show no evidence of inflammation, softening, or sclerosis.

The only noteworthy feature in the pons and medulla oblongata is degeneration of the pyramidal fibres. In sections prepared by Pal's method the pyramids appear completely degenerated, as seen with the unaided eye, but under the microscope many more or less normal fibres are seen scattered throughout these structures, while the myelin sheaths of many of the fibres which still stain are obviously greatly altered. All other tracts, such as the fillet, posterior longitudinal bundles, superior cerebellar peduncles, restiform bodies, and so on, show no evident departure from the normal.

What has been said with regard to the pons and medulla applies equally to the spinal cord, for in this part of the central nervous system the only abnormality that can be detected is degeneration of the crossed and direct pyramidal tracts. There is little difference to be made out in the amount of degeneration of the two crossed pyramidal tracts, but one direct pyramidal tract shows a more extensive area of degeneration than does the other, throughout the parts of the cord in which this degeneration is to be made out. As seen in the cervical region, the appearance of the two direct pyramidal tracts suggests that the one presenting the more extensive area of degeneration is in reality considerably larger than that of the opposite side; indeed, whereas the larger tract presents a convex border along the anterior median fissure, the corresponding border of the opposite tract is concave. The degeneration of the crossed pyramidal tracts can be traced throughout the cervical, thoracic, and lumbar regions of the cord to the sacral region, whereas the degeneration of the direct pyramidal tracts, as seen in sections prepared by Pal's method, can only be traced with certainty to the caudal end of the thoracic cord.

Optic Nerves.—Both optic nerves appear normal; there is neither any obvious degeneration of the nerve fibres, nor any increase of the interstitial tissue.

[In cases of cerebral diplegia, where the macroscopic condition of the hemispheres has been one of local or diffuse atrophy of convolutions, changes in the cells of the cortex, especially of the large pyramidal cells, without evidence of any vascular lesions or primary sclerosis, have been found by Cotard, in 1868; by Sachs, in 1892 (primary pyramidal neuron degeneration); by Warda, in 1895; by Mya and Levi (incomplete development of cells of motor zone), in 1896; and by Strumpell, in 1894.

In the rare and fatal form of familial diplegia associated with changes at the macular lutea, first described by Waren Tay, a similar degeneration of the cortical neurons has been found in every case investigated microscopically, as the sole pathological lesion.—J. S. C.]

Cases 3 and 4. Generalised Rigidity.

Isabel C., aged 2 years, and Kathleen C., aged 3 years, sisters, were admitted into the National Hospital on June 13, 1899, under the care of Dr. Ormerod, with paralysis "all over," dating from shortly after birth.

The parents were healthy, and there was no history of any nervous disease in their relations, nor any history of rheumatism nor tubercular disease. No history of syphilis could be obtained rom either parent on careful questioning. They had been married r nine years. Their first three children were born at full term, nd are perfectly healthy. The next child, K. C., was born at ght months, and weighed only three pounds at the time of birth. The mother had been "weakly" during the pregnancy. The birth was easy. The vertex presented; there was no asphyxia.

The next child, I. C., was also born at the eighth month, and was very small. There was considerable difficulty with delivery, apparently owing to uterine inertia, and instruments were used. The vertex presented, and there was no asphyxia. The mother was in a very weak state of health during the pregnancy.

The mother had received no injury during either pregnancy.

After the birth of the last child two miscarriages occurred, the first at the third month and the second at the sixth month. There was no assignable cause for the miscarriages.

The elder child, K. C., was apparently quite healthy at the time of birth. When two months old it was gradually noticed that though the child seemed quite intelligent, it could not use its limbs as it should have been able. Since this time the limbs have become more and more useless, and have become stiff. She never learned to talk. When two years old she had a general convulsion lasting half an hour, which the mother attributed to her having eaten some fruit. Her general health with this exception had always been good.

On admission she was a healthy-looking child, with an intelligent expression. She lay in bed with the arms flexed at the elbow and carried against the chest. The wrists were flexed and the fingers semi-flexed. The hips and knees were semi-flexed. She was not able to sit up, turn, or move in bed.

Her mental state seemed intelligent. She took note of everything around her, and smiled brightly when pleased; she understood simple speech. She occasionally cried, and when doing so gave vent to a series of hoarse, prolonged yells, unlike the crying of a healthy child. (This peculiarity was noticed in the four first cases reported in this paper.) She uttered no articulate sounds. The expression of the face was slightly fixed, and either angle of the mouth was dimpled in and rounded, evidently from tonic contraction of some of the muscles of that region. The head was a little retracted, and the muscles of the neck were distinctly rigid. There was some slight difficulty in swallowing.

The special senses, so far as they could be tested, were normal. The pupils were equal and reacted normally. There was slight divergent strabismus, but no nystagmus. The cranial nerves were normal. The teeth were ill-formed and carious. Th[illegible] muscles of the trunk were weak and rigid. She had no power [illegible] sit up or turn in bed. Both upper extremities were rigid at a[illegible] joints, but slight movement at all joints was possible, and s[illegible] could grasp a finger slowly. Marked athetotic movements of the fingers appeared when the limbs were moved about or tickled, the hands assuming the position of extreme flexion of the wrist and complete extension and spreading of the fingers and thumbs.

The lower extremities were semi-flexed at hips and knee, and there was contracture of calf muscles, flexors of knee and hip. There was much adductor spasm. There was slight pes cavus on either side. The legs were very rigid at all joints, and only the feeblest and most limited voluntary movements were possible. Sensation seemed unimpaired. The sphincters were normal. The plantar reflexes showed an extensor response on either side.

The abdominal reflexes were present. The knee-jerks were brisk. Foot clonus could not be elicited.

The position of this patient as she lay in bed was remarkable. The head and trunk were bent forward, and there was general kyphosis. The upper extremities were flexed across the chest, and the lower limbs drawn up by flexor contracture. This position is of frequent occurrence in cerebral diplegia, and has been described as the attitude occupying the least possible room. A similar attitude occurred in case 4.

The younger child, I. C., aged 2 years, was apparently quite healthy at birth, and seemed to progress well till about two months old. She was then noticed not to use the limbs properly. She had been getting progressively worse ever since. She had had two severe general convulsions, the first when a year old, the second when two years old.

On admission she was a healthy-looking child. Her symptoms and signs exactly resembled those of her elder sister, except that she had a convergent squint, and that the rigidity and athetosis were less marked and the power of moving the limbs a little greater.

There was the same expression of face with the angles of the mouth dimpled in, the same aphasia, head retraction, generalised rigidity, weakness and increase of the reflexes, extensor type of plantar reflex, and pes cavus, but these were less marked. This patient learned to say a few words when she was twelve months old, but afterwards she lost them, and had not uttered an articulate sound for nine months.

The chief points of difference between these two cases of generalised rigidity, and the Cases 1 and 2, are that in the former there was slighter involvement of the face and a higher degree of intelligence was preserved. Probably the cortical affection was resident chiefly on the central convolutions, excepting the facial and ocular region. The severe affection of the prefrontal and occipital lobes in the two first cases carrying with it an almost entire absence of intelligence was in these cases probably absent.

These cases were consecutive children of a mother who had suffered severely with general ill-health during both pregnancies. Both were born at the eighth month, and were very small. The difficulty in the delivery of the second child was evidently due to deficient power on the part of the mother. The two subsequent pregnancies terminated in miscarriages at three and six months respectively. Both cases presented symptoms from birth. It is here logical to consider the premature birth and the cerebral diplegia as concomitant effects of some morbid process affecting the mother during the pregnancies, and that the two subsequent miscarriages were attributable to the same cause.

Van Gehuchten has shown that the pyramidal fibres have not yet reached the lumbar cord at the seventh month of fœtal life, and, followed by Marie and Brissaud, considers that an arrest of development of the pyramidal tract occurs from the premature birth, and that the pyramidal tract fails to reach the lumbar enlargement, and so causes that form of cerebral diplegia known as "paraplegic rigidity," or Little's disease. This explanation of the pathology of paraplegic rigidity has received considerable acceptance among French writers on the subject, but it is based upon no pathological evidence. All recorded autopsies upon cases of paraplegic rigidity in children born prematurely have shown a very different pathological condition.

Cases of paraplegic rigidity in children born at term, either dating from birth or subsequently acquired, as in Case 5, and cases of generalised rigidity associated with premature birth, of which Cases 3 and 4 are examples, stand out in strong opposition to van Gehuchten's theory.

I submit that when cerebral diplegia occurs in association with premature birth, the two do not stand in causal relationship with one another, but are the concomitan[illegible] effects of a morbid process affecting both mother and fœtus

Case 5. Paraplegic Rigidity.

E. G., aged 6 years, was admitted into the National Hospital in March, 1899, under the care of Dr. Tooth. The father absolutely denied syphilis. The mother had had twelve children, of which the first eight were still-born at about the seventh month. The ninth child was this patient; the tenth died when a week old, the eleventh died of convulsions, aged two and a half years, and the last child was alive, but weakly, aged one year. She was a full term child, and the birth was natural. She had snuffles severely in infancy, and had measles when eighteen months old. Her health then remained good till four years of age, when she gradually became weak on her legs. In October, 1897, she had several attacks of left-sided convulsions, and the legs became gradually much weaker and became stiff. From this time she gradually became imbecile and passionate. She became unable to walk alone nine months after the legs were first affected. The left-sided fits continued at long intervals.

On admission she was semi-idiotic. The special senses, cranial nerves, and upper extremities were normal. The lower extremities were weak and rigid, with much adductor spasm, contracture of the ham strings and calf muscles, and double pes cavus. When supported she walked with a typical cross-legged gait. Knee-jerks brisk. Double foot clonus. The plantar reflex showed an extensor response on either side.

This patient showed no signs of congenital syphilis, yet from the history the presence of this factor is extremely probable. The common association of premature birth was absent in this case, yet the mother's first eight children were prematurely born. This history points most strongly to the diplegia and the premature births being the concomitant effects of some influence dominating both the development of the fœtus and the organism of the mother—perhaps, in this case, congenital syphilis. The congenital origin of this case is almost beyond doubt, notwithstanding that the patient enjoyed four years of apparent good health.

Case 6. Generalised Rigidity after long-standing Epilepsy.

C. F., aged 18 years, was admitted into the National Hospital on July 7, 1897, suffering with fits and paralysis all ver. There was a family history of asthma and rheumatism. He was brought up on the bottle, and in infancy had rickets and infantile convulsions and lasting nocturnal enuresis. When eight years old he fell a distance of twenty feet on to his head. A year later frequent attacks of petit mal occurred, and after another year these attacks gradually increased in severity until the fits reached the stage of severe general convulsions. He was an in-patient in the National Hospital on two occasions, in 1893 and again in 1895, on which occasion he was in the "status epilepticus" for several days. He had at this time no signs of organic disease. After his discharge in 1895 he slowly became stiff in all four limbs, and became unable to walk, and his mental state became dull. When admitted in 1897 he presented as a typical case of generalised rigidity. Mental state, semi-idiotic; mask-like face; optic atrophy; no strabismus nor nystagmus. All the limbs were very rigid, but there was no great loss of power. Double foot clonus. Knee, wrist, and elbow-jerks very much increased. The fits were very slight, general convulsive attacks lasting about half a minute.

Freud has suggested that the same morbid process to which cerebral diplegia is attributable may, when present in slight degree, be the cause of idiopathic epilepsy. In this case it is presumable that the functional changes in the cortical cells, expressing themselves in periodic epileptiform discharges, in the course of time were followed by structural degenerative changes, producing the clinical picture of cerebral generalised rigidity.

Since epilepsy is held to be a disease of the cortical neurons, it may be justly inferred that the pathological process giving rise to the generalised rigidity was the same in this case as was found by Dr. Russell in Cases 1 and 2, *i.e.*, slow degeneration of the cortical neurons.

Case 7. Generalised Rigidity occurring in an Adult.

A. B., aged 28 years, was admitted into the National Hospital, under the care of Dr. Tooth, on March 17, 1899, complaining of stiffness "all over," slowness in the execution of all movements, and "trembling of the eyes." The symptoms had come on gradually and progressively during the last three years.

He was an only child. There was no history of nervou disease in his family, who were very healthy people. There wa nothing in the history to suggest that he had been the subject o hereditary syphilis.

Up to the commencement of this illness he had never ailed for a day, with the exception of measles in childhood and a slight attack of influenza in 1892. He denied syphilis, and also exposure, and his habits were abstemious as regards alcohol. He had been employed as a gardener, and had worked a good deal under glass. He had had no injury of any sort.

The history of the illness was as follows:—

In March, 1896, he noticed pain and numbness in the legs, which felt weak when he walked upstairs. He also noticed at this time that when his hands remained still for some time, as, for instance, on waking in the morning or after walking with his hands in his pockets, that they became stiff and numb—a condition which passed off in a few minutes if he moved them vigorously. He did not notice anything wrong with the hands when he was at work. Two months later he noticed stiffness of the face, and his friends told him that his eyes trembled (spontaneous nystagmus). For the next eighteen months the stiffness spread slowly all over the body, and his limbs became weaker. At the end of this time he became much worse in the course of a few weeks, and he became unable to loose his hold upon objects when he had grasped them. The face, neck, trunk, and the four extremities were at this time very rigid, and the rigidity was not lessened by active or passive movements. All movements became slow, and he had to give up work. The left limbs were more severely affected than the right, and he dragged the left foot in walking. He felt his face stiff in laughing, and had difficulty in swallowing. For the last year his condition has been improving very slightly.

His general health throughout the illness had been good. He complained at times of severe pain in the left shoulder and hips; referable to the condition of left hemiparesis. He had had no pyrexia, and no fit of any sort, nor had he had any other symptom referable to any toxic agent.

On admission he was a sparsely nourished, sallow-complexioned man. His appearance was remarkable. He had a dull mask-like unvarying expression, resembling that of Parkinson's disease, with a marked convergent strabismus and incessant spontaneous lateral and rotatory nystagmus. As he stood, all the visible muscles of the body showed fibrillary twitchings. The head was carried stiffly and bent forward on to the chest. He could get about with some difficulty, and could feed himself slowly, but he could not dress himself. He felt perfectly well in himself.

He was a very intelligent man, and his memory was good. His speech was monotonous, and he moved his jaw and his lips very little when he spoke. He said that since his illness his voice had quite altered. The special senses and optic discs were normal. The pupils were equal and reacted normally. There was an old convergent strabismus, the left eye being at fault, dating from measles in infancy.

With the exception of the nystagmus and the stiffness and slowness of movement of the face and jaws, the cranial nerves were normal.

The neck was very rigid, and the sternomastoids stood out in strong spasm, causing the neck to appear much broader than natural. Movements of the head upon the trunk were stiff and slow.

All the muscles of the trunk were hard and board-like to the touch, and movements were stiff and slow. He could not get up out of a low chair without assistance. Respiratory movements seemed somewhat confined in range, but were otherwise normal.

The muscles of the upper extremities were small and hard, but there was no localised wasting. There was great rigidity at all joints. The terminal phalanges of the fingers were sharply flexed on the second phalanges, and semi-flexed at the other joints. The left arm was carried pressed into the side with the elbow flexed to a right angle (the position common in hemiplegia). All movements were performed stiffly and slowly, but with considerable power; but when he grasped an object he was unable to relax his grasp for some considerable time and after much evidence of effort. Having flexed either elbow forcibly, he was entirely unable to extend it for some seconds, and having extended was unable to flex for a similar period.

He complained of considerable pain on passive movement in the left shoulder.

Both lower extremities were stiff at all joints, and movement was slow, but all movements could be performed with some power. There was the same difficulty with the relaxation after effort as was seen on the upper limbs. The left leg was throughout weaker and stiffer than the right. He walked stiffly with small steps, and dragged the left foot. There was no preponderating flexor or adductor spasm.

The electrical reactions of the muscles of limbs, trunk, and face were normal.

Sensation was unimpaired. The lightest touches and pricks were everywhere felt and localised accurately. The temperature sense was normal. The sense of position was acute. The sphincters were not affected. He perspired profusely, especially on the limbs. The knee-jerks were very brisk. Foot clonus could not be obtained, probably owing to the rigidity. The phantar reflex showed a marked extensor response on either side.

The cranium and spine were normal, and the thoracic and abdominal viscera presented no peculiarities. He was treated with hot alkaline baths, massage, passive movements, and

Kepler's extract, and the slowness of movement improved slightly during his stay of four months in the hospital.

This case presents all the typical signs of cerebral generalised rigidity, with the exception of intellectual impairment. Very few cases of cerebral diplegia occurring in adult life have been recorded. The clinical resemblance between the case and the preceding cases of generalised rigidity is very striking, and the disparity in severity of the symptoms and as regards intellectual impairment becomes less if it be taken into consideration that the incidence of the disease in the children was upon a functionally non-developed nervous system, and in this case upon a nervous system at the height of its functional activity. The spontaneous nystagmus, mask-like expression, altered voice and dysphagia were indicative of loss of the action of cortical centres upon the nuclei of the cranial nerves, and are spastic signs in the region of the cranial nerves comparable with, and of like significance to, rigidity and increase of the deep reflexes in the limbs.

The case bears a certain resemblance to one of paralysis agitans in the expression, alteration of voice, rigidity of the trunk, and slowness of movement.

The latter disease is, in all probability, a cerebral diplegia of a special type.

I submit that this case was one of slow degeneration of the cortical neurons of the central convolutions.

Weill has recently published a remarkable case of diplegia generalised rigidity, in which rhythmic tremor of the hands and forearms, exactly resembling those of Parkinson's disease, appeared. A healthy girl, aged 10½ years, was seized with violent cephalagia, followed a fortnight later by complete paralysis of all the limbs. A month later she began to improve, and her resulting state was as follows:—Intelligence perfect. Mask-like face. Parkinson's attitude. Generalised rigidity. Rhythmic tremor of forearms and hands. Right-sided hemiparesis. Right talipes equinovarus. Athetotic movements of feet. Subjective sensation of heat in the limbs.

Weill states that cases clinically correcting cerebral diplegia and Parkinson's disease occur.

PART II.— AN ACCOUNT OF CEREBRAL DIPLEGIA.

The clinical picture of cerebral diplegia was first recorded by Andry in 1741. Delpech, in 1828, described a case, but it was not until 1853 that general attention was called to this clinical group by Little, to whose accurate clinical descriptions of both the generalised and paraplegic forms there has remained little to be added. He associated choreic types and bilateral athetosis with diplegia. He drew attention to the close connection of these cases with premature and difficult birth and with asphyxia neonatorum. The name "Little's disease," was suggested by Rupprecht in 1888, and has since been generally used for all forms of infantile cerebral diplegia. Recently an attempt has been made by van Gehuchten and Brissaud to confine the name, "Little's disease," to paraplegic forms of diplegia, on the ground that this syndrome, first described by Little, is a separate entity from other forms of diplegia, and that it has a special ætiology and clinical aspect. Heine, in 1860, described cases under the name of cerebral spastic paraplegia. Erb, in 1877, considered the paraplegic forms to be of spinal origin, using the term, "tabes dorsale spasmodique." Ross pointed out the cerebral origin of purely paraplegic forms in 1885.

In 1884 Strumpell aroused great interest in the pathology of the disease by his description of acute polio-encephalitis. Though Strumpell's acute encephalitis has fallen to the ground as the initial lesion in cerebral diplegia, the attention and controversy aroused by his work have been of great importance in furthering our knowledge of the morbid anatomy of the disease. The pathological condition he described in his cases has been found connected with a special symptomatology, and the disease, acute non-suppurative encephalitis, has been placed upon a firm basis.

In 1882 a valuable contribution to the pathology of the disease was made by Kundrat in his work on porencephaly.

The literature of the subject during recent years has been very extensive. The most important summaries are monographs by Andry on porencephaly, in 1888, and on choreic forms, in 1892; by Lannois, in 1893; by Rosenthal (with bibliography), in 1893; an exhaustive treatise upon infantile cerebral paralysis, with a complete bibliography by Freud, in 1897, and the article by Sachs in his "Treatise on the Nervous Diseases of Children," 1895.

Recent contributions to the pathology of the disease have been made by B. Sachs, Hirsch, Kingdon and Russell, van Gehuchten, and Massalongo.

The Clinical Types of Cerebral Diplegia.

Infantile diplegia is separated both ætiologically and clinically from infantile hemiplegia, though in rare cases the two conditions may co-exist. Ætiologically, the diplegias are for the most part congenitally determined diseases, the hemiplegias for the most part acquired diseases. In diplegia rigidity or perverse movement preponderates over paralysis, and dominates the clinical picture, while, in hemiplegia, paralysis dominates the clinical picture, and the rigidity is secondary to the paralysis. The preponderance of the affection of the arm, which is the rule in infantile hemiplegia, is scarcely ever present in diplegia. In accordance with these facts, the sharp distinction between cerebral diplegia in its generalised form and bilateral spastic hemiplegia, which is laid down by French and German authors, is justifiable and clinically useful. While it is impossible to distinguish clinically between the most severe forms of generalised rigidity and bilateral spastic hemiplegia, where the paralysis is complete, in the majority of cases the distinction is quite easy. For the purpose of this distinction it is perhaps useful to retain bilateral spastic hemiplegia in a classification of the clinical types of cerebral diplegia. A clinical classification of the forms of cerebral diplegia is the only one of any value. The disease forms at present a clinical and not a pathological entity, and its type is determined by other than the hitherto discovered morbid anatomical factors. It has been up to the present time impossible to determine from the *post-mortem* appearances whether the clinical aspect of a given case had been one of generalised rigidity, or paraplegic rigidity, or bilateral athetosis, or of choreic diplegia. A classification based upon morbid anatomy is, therefore, impossible. On account of the obscurity of the ætiology and the diverse opinions held by authorities concerning the origin of the disease, a classification on ætiological grounds is at present impossible.

The classification here adopted follows that of Rosenthal:

(1) Generalised rigidity.
(2) Paraplegic rigidity.
(3) Bilateral spastic hemiplegia.
(4) Bilateral athetosis.
(5) Choreiform diplegia (congenital chorea).[1]
(6) Atypical forms (slight generalised rigidity with profound mental changes).

With the exception of bilateral spastic hemiplegia every form of transition between the other five types is met with, and many varieties of combinations of these types.

The following table shows the relative frequency of the clinical types as observed by Rosenthal, Sachs, and Petersen, and in the cases I have seen in the wards of the National Hospital:—

	Rosenthal.	Sachs and Petersen.	Cases in National Hospital, 1898-9.
	53 cases.	69 cases.	23 cases.
Generalised Rigidity	27	39	9
Paraplegic Rigidity	13	30	4
Bilateral Spastic Hemiplegia	3	..	1
Bilateral Athetosis	3	..	3
Choreiform Diplegia	3	..	3
Atypical Mental forms	4	..	3

Clinical Ætiological Factors.

Of the recorded cases of cerebral diplegia 66 per cent. show some definite clinical antecedent apparently in causal relation with the disease, while in 33 per cent. this is entirely wanting.

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[1] Rosenthal uses the term "chorée generalisée" for this type which has hitherto been called "congenital chorea" by English writers. As these terms do not suggest the intimate connection of this condition with the other types of diplegia, and as both are somewhat inaccurate since the so-called choreic movements are, as a rule, not generalised, and the cases not always congenital, I venture to submit the term choreiform diplegia for this type as being a convenient one.

The attributed ætiological factors are here summarised:—

(1) Maternal pathological states during pregnancy: general ill-health, syphilis, specific fevers, eclampsia, pathological psychic states, and injury to the abdomen.

(2) Abnormalities of birth: premature birth, birth injuries, prolonged labour, precipitate labour, asphyxia neonatorum.

(3) Heredity, and consanguinity of parents.

(4) Post natal pathological conditions: Acute infectious diseases and acute fevers, vascular lesions, epilepsy, acute encephalitis.

It is essential to bear in mind in the consideration of these attributed causes that more than one of these factors may be present in a given case, and that it is probable that many of the abnormalities of birth stand not in causal relation with the disease, but as concomitant effects of a morbid maternal state. It is certain also that some of the post-natal factors are immediate precipitating factors, bringing into evidence a congenitally installed disease.

Maternal Pathological Conditions.

A history of ill-health of the mother during pregnancy is common in cases of diplegia. The mother often volunteers the statement that while she was perfectly well and strong during her other pregnancies, her health failed completely during the carriage of the child afflicted with diplegia. Overwork and privation sometimes account for this failure of health. Several recorded cases give this history that a woman after bearing healthy children suffers with symptoms which may be described as those of chronic neurasthenia. She then gives birth to a child afflicted with diplegia, and her subsequent pregnancies end in still-births. (*Vide* cases 3 and 4.) This seems to show a gradual failure in the physiological process of generation. In support of this suggestion it has been pointed out by most authors who have written on the subject that the youngest members of large families are especially prone to suffer.

In some cases a pathological psychic state of the mother during the time of pregnancy has been noted. Acute diseases and acute specific fevers occurring during pregnancy are of great importance as ætiological factors in this disease. I have twice obtained a history of eclampsia not followed by premature birth in cases of paraplegic rigidity, and in one of these cases the eclampsia followed an attack of scarlet fever.

Syphilis is a most important and by far the most common maternal disease standing as a causal antecedent to cerebral diplegia. Many cases have been recorded by Gasne, Gaudard, Gee, Moncorvo, De Amicis, Jendrassik, Marie, Haushalter, Fournier, and others. Brissaud considers syphilis only a factor in that it causes premature birth, and he considers diplegia to be the result of premature birth. With more justice Gasne argues that premature birth should be ignored as a factor, and he considers that syphilis or some other toxic process is responsible for the production of diplegia and of premature birth in cases where these are associated.

The percentage, however, of cases of diplegia in which a history of parental syphilis is obtained is small. Freud considers that this small percentage is due to the fact that so many children infected with syphilis are still-born.

In connection with the pathology of meningeal hæmorrhage attention will be drawn again to syphilis as a cause of diplegia.

Tubercular disease of a severe nature was present during pregnancy in cases reported by Levi-Sirigue and Haushalter.

Injury to the fœtal head in utero must be here mentioned as a possible factor. Such injury has been proved in some cases of infantile hemiplegia. Gibb, quoted by MacNutt, reports a case of intra-uterine hemiplegic atrophy, with contracture, in a still-born child. A meningeal hæmorrhage was found accounting for the condition. As a factor of meningeal hæmorrhage trauma to the fœtal head in utero may be a cause of diplegia.

It has been repeatedly observed that where one child of a family is afflicted with diplegia, the mortality among the other children is remarkable, and premature birth is common. (Freud, Graef, and Little.)

Abnormalities of Birth.

Premature birth occurs very frequently in association with all forms of diplegia, and most often in connection with paraplegic rigidity, and it has been considered a factor in the production of the disease by many writers. Van Gehuchten, Marie, and Brissaud consider that an arrest of development of the pyramidal tracts in the spinal cord occurs as a result of the premature birth and that this is due to post-natal claims upon nutritive functions, rigidity ensuing from the unrestrained action of spinal centres. Since the pyramidal tract has only reached the medulla at the seventh month of fœtal life, according to these authorities premature birth at that time will cause generalised rigidity. At the eighth month the pyramidal tract has reached the dorsal region, therefore premature birth at that time produces paraplegic rigidity. After birth some slow renewal of the arrested growth of the pyramidal system occurs; therefore these cases tend to improve. Van Gehuchten's theory does not accord well with pathological and clinical facts, and the very arguments he uses to advance this theory, which is based on no pathological evidence, prove fatal to it. Diplegia occurs only in an immense minority of prematurely born children; it is frequently unassociated with premature birth, and frequently is of post-natal onset. There is proof that tracts in the central nervous system develop normally after birth, for instance, the cerebral association systems. The pyramidal system is not completely myelinated at full term. The recorded autopsies upon cases of paraplegic rigidity, for example, those of Förster and Sachs, have revealed gross cerebral lesions. That cases of paraplegic rigidity tend as a rule to improve is certainly not the experience of most observers. The arguments against this theory may be multiplied almost indefinitely if the history and clinical facts of cases of paraplegic rigidity be considered from the standpoint of van Gehuchten's theory of the pathology of the disease.

The balance of the evidence on record is in favour of the opinion held by Gasne, Marfan, and Freud—that premature birth does not stand in causal relation with diplegia, but is a concomitant effect of the morbid process in which diplegia has its origin.

Birth injuries have been placed in a very prominent position among the clinical antecedents of cerebral diplegia ever since Little drew attention to the association, and the clinical type—generalised rigidity—has been made dependant upon birth injuries. This view was strongly upheld by Gowers, and has been followed by Marfan and Raymond, and recently by Taylor.

The association of precipitate birth, prolonged birth, instrumental birth, and asphyxia neonatorum with diplegia, especially with the type generalised rigidity, is very common. This association was present in 72 per cent. of Rosenthal's cases.

Kundrat believes that precipitate labour is equally potent to produce diplegia as is prolonged labour and asphyxia neonatorum, and Tyler Smith considered that the absence of gradual adaptation of the fœtal head to the pressure exercised upon it by the parturient canal and the rapid alterations of that pressure during parturition gave rise to meningeal hæmorrhage. Difficult and prolonged birth are considered to produce meningeal hæmorrhages by causing undue lapping over of the parietal bones along the sagittal suture and rupture of the veins emptying into the superior longitudinal sinus (Virchow and Weber). This lapping takes place to a greater extent when the head is after coming, and therefore diplegia is more frequently associated with breech presentations than vertex presentations. The meningeal hæmorrhage from this cause will be bilateral, and will affect the paracentral lobule first and most; this explains the preponderating affection of the legs in many cases, and the bilateral symmetry of the disease. The gradual tailing off of the meningeal hæmorrhage across the central convolutions towards the Sylvian fossa is responsible for slighter affection of the upper limbs, and still more slight affection of the face. The larger size of the fœtal head in male children and consequent greater compression in labour has been brought forward by James Taylor as an explanation of the preponderance of males in his statistics of cases of diplegia.

Asphyxia neonatorum is considered to be an important agent in producing meningeal hæmorrhage, and from that cerebral diplegia. Little has pointed out that most infants presenting asphyxia at birth are not affected. Direct injury to the brain or meninges from the pressure of the forceps has not been shown in any recorded case of diplegia.

There are very great difficulties standing in the way of the general acceptance of birth injuries and meningeal hæmorrhage as causal factors in the production of diplegia, notwithstanding their frequent association. The importance of these conditions as factors has probably been greatly over-estimated. The pathological objections are serious and will be detailed in that part of this communication dealing with the pathology of diplegia.

Clinically this explanation of the ætiology is insufficient. It does not account for cases associated with birth difficulties where the symptoms of diplegia do not appear till some months after birth, nor for the so-called acquired cases. In 28 per cent. of Rosenthal's cases there was no abnormality of birth or asphyxia. Of three cases of diplegia of the same clinical type occurring among the children of one mother one case was associated with difficult labour and asphyxia neonatorum, and would have served the supporters of this view as a typical case of meningeal hæmorrhage producing diplegia. The other cases, however, showed no abnormality of birth. In one the symptoms appeared at birth and in the other at seven months of age (Feer).

A somewhat similar history occurred in my cases 3 and 4. The bearing of such cases upon the acceptance of this explanation is obvious.

Ganghofner and Freud are the chief opponents to the origin of cerebral diplegia in meningeal hæmorrhage, and the latter points out that severe injuries to the fœtal head are often without effect in producing diplegia, and that cases are probably congenital in spite of Little's factor. He says: "Difficult birth and asphyxia neonatorum are themselves only symptoms of deeper lying influences which have dominated the development of the fœtus or the organism of the mother."

Consanguinity of the parents has been recorded in cases of cerebral diplegia by Brissaud, Haushalter and Dejerine.

Oppenheim reports a case where a mother and her daughter were similarly affected with cerebral diplegia.

Post-natal Ætiological Conditions.

In the consideration of cases of cerebral diplegia arising after birth, stress must be laid upon the fact that the post-natal appearance of symptoms of disease is no proof that the disease was not congenitally determined. The possibility of an acute disease immediately preceding the onset of symptoms being in some cases only an immediate exciting cause bringing into evidence a latent pathological condition, must also be borne in mind.

Most cases of post-natal cerebral diplegia do not follow any known acute disease. Cases have been reported in which the onset of symptoms directly followed the occurrence of the following acute diseases :—gastro-enteritis (Marfan, Massalongo, Rissler), scarlet fever, measles, mumps, pneumonia, acute rheumatism, typhoid (Massalongo), diphtheria (Massalongo), and influenza (Massalongo).

The onset of cerebral diplegia with acute febrile symptoms was attributed by Strumpell to acute polioencephalitis. This assumption has not been confirmed by subsequent investigations. More recently Massalongo has brought forward acute toxic meningo-encephalitis as a cause of these symptoms.

Symptoms pointing to vascular lesions, thrombosis and embolism and hæmorrhage may occasionally precede the syndrome of diplegia. Undoubted cases of multiple embolisms have been recorded by Heubner and Abercrombie, and of thrombosis by Abercrombie and Angel Money. Gowers thinks that sinus thrombosis and thrombosis of the surface veins account for some of the cases, but this has only been demonstrated pathologically in one case of Abercrombie's. In Ashby's case the condition found after death (multiple cysts), was considered to be the result of multiple hæmorrhages. Sachs and Petersen consider that intra-cerebral hæmorrhage is an important cause of acquired diplegia.

Epilepsy of long standing may be followed by cerebral diplegia as in Case No. 6 here reported.

Hydrocephalus occurs sometimes in association with cerebral diplegia, especially with paraplegic rigidity. The paraplegia is here referable to some localised pathological condition of the cortex which is not dependent upon the condition of ventricular distension. The latter frequently exists without any such symptoms.

Summary.

One-third of the recorded cases of cerebral diplegia are without known clinical antecedents.

Maternal morbid states are probably by far the most important clinical antecedents, and such states have probably existed in many of the cases to which no definite cause can be assigned.

Premature birth has probably no causal relation with diplegia.

The causal relation of birth injuries and asphyxia neonatorum to this condition has been much over-estimated, and the absolute proof of it is as yet wanting, notwithstanding the frequency of the clinical association.

Some cases certainly follow cerebral vascular lesions.

Acute diseases sometimes precede the onset of symptoms, but whether in all cases as the initial factor in disease, or in some cases only as an immediate exciting cause, has not been determined.

Clinical Aspect.

In the majority of cases of generalised rigidity and in athetotic and choreic diplegia, the symptoms date from birth. Often in slighter cases the symptoms are only manifested when the child begins to crawl about or to walk. The attention of the parents may be drawn to the fact that something is wrong with the child by its being backward in talking and mentally unlike other children, and examination may then reveal slight generalised or paraplegic rigidity. The nurse, in washing the child, is often the first to notice the unnatural stiffness of the limbs. In congenital athetotic and choreic forms, the symptoms become much more evident when the child begins to get about. In cases where the symptoms are noticed first some time after birth, a careful attention to the history of the case will generally reveal some abnormality of the child, indicating that the case was congenital, and separating it from cases of post-natal origin. Such symptoms, as difficulty of swallowing, strabismus, nystagmus, slight perverse movements (choreic and athetotic), slight rigidity, the regular assumption of an unnatural attitude, and pes cavus, are likely to be noticed by those who tend the infant, and are of great value in that they may be the earliest signs of disease to attract attention.

In post-natal cases the disease is often ushered in by a group of symptoms resembling the prodromal symptoms of acute anterior poliomyelitis, namely, malaise, anorexia, headache, slight fever, and sometimes vomiting. These symptoms last from one to four days, after which the symptoms of diplegia gradually make their appearance. The onset of the disease is frequently with convulsions, either a single attack of convulsion or repeated attacks. In 37 per cent. of the cases collected by Freud, and in 50 per cent. of those of Rosenthal, the onset of the disease was marked by convulsions. After such convulsions the symptoms of diplegia may come on slowly, or may develop from a condition of general paresis of the limbs and trunk, which immediately follows the convulsive attack. Sometimes both convulsions and febrile symptoms, lasting a few days, occur at the commencement of the disease, and this has been more often noticed in cases of post-natal paraplegic rigidity. In other cases the onset is gradual, and is not accompanied either by convulsions or febrile symptoms, and it may be many weeks before the symptoms reach moderate intensity. Such chronic onsets sometimes date from some trauma to the head, often of a trifling nature. A slow onset without definite initial symptoms is the rule in the few reported cases commencing after childhood.

The course of the disease, speaking generally of all types, may be either regularly progressive, or the symptoms, having reached a certain degree of intensity, may either remain stationary or tend to some slight amelioration. In severe cases of generalised rigidity, and in most athetotic forms, a progressive course is the rule, and very few patients so afflicted reach adult life. In the familial variety of generalised rigidity described by Waren Tay, Sachs, Kingdon, and Russell, the disease is always rapidly progressive to a fatal termination.

A tendency to amelioration is sometimes seen in cases of slight generalised rigidity and in cases of paraplegic rigidity, but in even the slightest cases the amount of improvement is not great, and the symptoms never entirely disappear.

Between the several types of cerebral diplegia there exists every variety of transitional form and combination.

The clinical picture of cerebral diplegia, in all its forms, presents a combination in varying degrees of certain characteristic symptoms; always bilaterally represented, though often more severe upon one side of the body than the other. These symptoms are:—Muscular rigidity, paresis, perverse movements, contractures, and increased deep reflexes.

To these symptoms, notwithstanding the opinions of van Gehuchten, Marie, and Brissaud, should be added mental deficiency, evidence of which, I think, can be obtained in almost all cases. In their attempt to separate off congenital paraplegic rigidity as a distinct clinical and pathological entity, and to confine to that entity the term "Little's disease," these authorities lay stress upon the absence of mental symptoms in paraplegic rigidity. Slight cases of paraplegic rigidity on reaching puberty always show the poorest intellectual capacity, and from this level of mental deficiency there is every gradation downwards to complete idiocy to be found among such cases.

The appearance of those suffering with this disease has been described by Shakespear in Richard III., Act i., Scene 1, and by Sir Walter Scott in "The Pirate" (Nick Strumpfer the dwarf), and Raphael has painted the picture of the disease in his "Transfiguration" (Lannois, Ross, Freud).

Generalised Rigidity.

(Gr. Allgemeine cerebrale starre; Fr. Rigidité generalisée.)

As its name implies the chief characteristic of this type of diplegia is a condition of muscular rigidity associated with weakness, affecting to a greater or less extent all the muscles of the body. Except in the most severe cases where the weakness amounts to complete paralysis there is more rigidity than weakness. In some cases it is astonishing that there should be so much power in the presence of such a degree of rigidity. The distribution of the rigidity and weakness is generally that the lower extremities are most affected, the upper to a less degree and the facial region still less. In a few cases (Rosenthal and Freud) the arms have been more affected than the legs. Paroxysmal exacerbations of the rigidity have been noticed by Money and Ganghofner. Movement is slow and clumsy, and often athetotic and choreic movements are present in the limbs. If the patient is able to walk, the gait is digitigrade from contracture of the calf muscles. The knees are slightly flexed from contracture of the hamstrings. The thighs are rotated inwards and the knees pressed close together, rubbing against one another with each projection of the limb. More severe adductor spasm gives rise commonly to the "cross legged" progression.

The assumption of the sitting position is impossible in marked cases. When such a patient is placed in a chair the legs stand out stiffly, and the child will not fit the chair, owing to the rigidity preventing the necessary flexion at the junction of the lower extremities with the trunk; he tends therefore to slide off. In the most severe cases the patient lies in a log-like fashion, unable to move or turn in bed, and then the rigidity may reach such a degree that he may be lifted by the heels in one rigid piece, the weight of the body being supported on the back of the head. In this stage, owing to muscular contractures, certain characteristic attitudes are assumed which will be described later on.

After this brief, general description, it remains to discuss the symptoms in detail.

Mental Symptoms.

Every degree of mental impairment is met with in these cases, from slight mental dulness to complete amentia. As a rule the average degree of mental impairment is more profound than in the other types of diplegia. It, however, does not always correspond to the severity of the rigidity and paralysis. The most profound mental deficiency may exist in cases where the rigidity and paralysis are quite slight and *vice versâ*. This corresponds with the greater or less affection of the præ-frontal lobes. The amount of mental impairment must not be estimated from the facial expression, as conditions of facial over-action and rigidity, perverse mimetic or athetoid movements of the face may lead to an opinion that there is much greater mental impairment than exists in reality. The mental state is, as a rule, placid. Some of the slighter cases are irritable, mischievous and passionate.

Speech Defects.

In congenital cases, and in cases occurring before the eighteenth month, speech may never be acquired, or may be much delayed, and when acquired is often imperfect. A patient of Dr. Bastian's, recently in the National Hospital, began to utter articulate sounds for the first time at nine years of age. Articulation is imperfect, slowness of speech with great facial over-action, slurring and stammering often occurs. According to Ganghofner, 59 per cent. of cases of diplegia (all types) show marked speech defects. When the disease arises after speech is learnt it is generally completely lost if the child be younger than six years of age, and if the case be at all severe. The loss of speech may be quite gradual, and where some intelligence persists the understanding of words may remain in patients who can utter no articulate sound. This was certainly ascertained in two of the cases recorded here (Cases 3 and 4).

Under this heading I may mention the curious and characteristic manner in which children affected with severe generalised rigidity cry. They give vent to a series of hoarse prolonged roars very unlike the screaming, sobbing and broken respiration of a normal child. This peculiarity has been present in all the cases of generalised rigidity in children that I have observed, notwithstanding that in some of them a moderate degree of intelligence was preserved.

Convulsions.

With this type of cerebral diplegia convulsive attacks are more commonly associated than with the other types, choreic diplegia and bilateral spastic hemiplegia being excepted. They occur in rather more than half the cases (Rosenthal).

In 50 per cent. of the cases presenting a history of convulsions, several attacks of convulsions occurred and in 25 per cent a regular epilepsy became established or 12·5 per cent. of all cases (Rosenthal). It may then be stated that epilepsy is not of usual occurrence in cases of generalised rigidity. It is interesting to compare both the initial convulsions ushering in the symptoms in undoubted prenatally installed cases, and the subsequent infrequent convulsive attacks to the convulsive seizures occurring in cases of general paralysis of the insane. I would here suggest the possibility that such attacks may have their origin in the same morbid physiological process in the two diseases.

In cerebral diplegia convulsive attacks have no connection whatever with a traumatic origin of the disease. Nor do they bear relation for the most part with the severity of the other symptoms. Osler states that in cases of slight diplegia every symptom may disappear except the epilepsy.

Special Senses.

Primary optic atrophy occurs in a considerable number of cases. Of seventy-two cases observed by Koenig, twelve presented marked optic atrophy, and in two of the cases it was unilateral. It may produce complete blindness. In the familial type of generalised rigidity of Waren Tay, and Sachs, a peculiar form of degeneration of the retina was found in all cases. In these cases a whitish-grey oval patch was seen almost twice the size of the optic disc, with softened edges and with its long axis lying horizontally, very slightly raised above the general surface of the retina. The fovea centralis was seen as a cherry-red spot in the centre of this area. Holden found this appearance due to primary degeneration of the ganglia cells of the retina. Waren Tay observed slight optic neuritis in one of these cases. In all these cases marked optic atrophy appeared, and in time produced complete amaurosis. Attention has also been drawn to optic atrophy by Feer, Moeli, Freud and Koenigsbeer.

Cranial Nerves.

Inequality of the pupils and slowness of the light reaction are not uncommon. Spontaneous nystagmus of very wide range is common in cases where the face is markedly affected. It is to be regarded as the spastic ocular sign analagous to the rigidity elsewhere, and produced in the same manner (Osler, Sachs, Koenig, Freud, Rosenthal).

Convergent strabismus occurs in about 30 per cent. of the cases (Freud). Rosenthal considers that this symptom is produced by a concomitant lesion in the region of the third nerve nucleus, but this conception rests upon no pathological evidence.

In nearly all cases the face shows signs of paresis and rigidity. With slight involvement of the face this may be shown by a general loss of emotional expression, slight retraction of the eyelids and some retraction of the angles of the mouth. With more severe involvement of the face an unvarying starched expression with wide palpebral apertures and a large open mouth (*bouche en cœur*) are present. The facial aspect then resembles strongly that of paralysis agitans. Slobbering is common. In some cases involuntary facial overaction is present and gives rise to varying grimaces on attempts to move the face or on speaking. Athetoid movements of the face are not rarely seen.

The tongue is often very large and the hard palate very much arched. The presence of adenoid vegetations in the pharynx is frequently noticed.

Difficulty of swallowing is present in the large majority of cases, though it may be slight. On watching the act of deglutition in these cases the difficulty seems due to rigidity of the muscular apparatus rather than to any paralysis. Little was the first to observe dysphagia in this disease. Recently Koenig has stated that slight bulbar symptoms are always present, and this may be said to hold good for all the types of diplegia. Cases with severe difficulty in swallowing have been described by Oppenheim under the name of "infantile pseudo-bulbar paralysis."

There may be difficulty with protrusion of the tongue and this organ usually shares in the facial athetosis, if this is present.

Laryngeal difficulties, dysphonia, stridor, &c., have been noticed by Levi-Sirigue.

Conformity of the Skull.

In congenital cases microcephaly is generally present (25 per cent. of all cases, Rosenthal). Signs of hydrocephalus are present in some cases. Asymmetry and flattening of the region of the central convulsions are common (Fischer and Peterson). In a case of slight generalised rigidity with profound mental changes I have noticed the frontal region small and flat disproportionately to the rest of the skull. In another case under my care of slight generalised rigidity, where speech was retarded till the ninth year, great flattening of the left frontal region and of the right cerebellar region was present. In a few cases a defect in the skull in the central region through which the brain could be felt to pulsate has been found.

Autopsies upon such cases have shown a porencephalic defect underlying the hole in the skull (Ross and Meschide).

Attitude.

In the more severe cases characteristic attitudes are assumed. The head may be rigidly retracted, but more commonly the chin is pressed down upon chest. Torticollis has been noticed in two cases by Rosenthal. In a case at present in the National Hospital, under the care of Dr. Beevor, the onset of the disease occurred at 12 years of age with convulsions and fever. A week later torticollis was noticed, which became severe in three months and then gradually lessened, but was still evident eighteen months later. The case was a combination of slight generalised rigidity with severe paraplegia rigidity.

The spinal column generally shows kyphosis, sometimes lordosis, and often scoliosis.

The cases presenting lordosis usually have head retraction, and those with kyphosis a flexed position of the head.

Several characteristic attitudes have been described and named, and these occur with sufficient frequency to deserve special note.

(1) *The Cramped Attitude* (*Freud*).—The head and trunk are bent forward. There is kyphosis. The elbows are pressed into the sides and the forearms crossed on the chest in contracture. There is contracture in the fully flexed position at hip and knee joints. The position has been described by Freud as that in which the patient occupies the least possible space.

(2). *The Attitude of Adoration* (*Freud*).—The head is retracted and the eyes are staring. There is lordosis. The elbows are pressed into the sides and the hands are held supinated below the face. The legs are rigidly extended.

(3) *The Extension-supination Position.*—The limbs are rigidly extended and the forearms are fully supinated. More rarely extreme pronation is associated with the extended position of the limbs.

Pes cavus is present in most of the cases. Some cases show a condition of talipes equino-varus. Genu recurvatum sometimes occurs.

The mode of progression in these cases where any is possible is characteristic. Little compared the gait to that of the tardigrade animals. The "cross-legged" progression is so well known as to need no description here. Where the legs are so severely affected as to render walking impossible while fair power remains in the upper limbs the patient may crawl along the ground with the upper limbs dragging the useless lower limbs and trunk. This has been termed by Freud the "broken-backed" progression from its resemblance to the progression of a broken-backed rabbit. This last description applies more to the type to be later described as paraplegic rigidity than to generalised rigidity.

Muscles.

In some cases a curious hardness and resistant feeling of the affected muscles is present resembling a similar condition in pseudo-hypertrophic paralysis. If athetosis is associated with the rigidity there may be actual hypertrophy of the muscles.

In late stages of severe generalised rigidity the muscles are always wasted.

In the rapidly fatal cases of Waren Tay and Sachs, the muscles waste rapidly, although the normal responses to electrical stimulation are preserved, and there may be associated with this wasting complete flaccidity of the muscles. Fibrillary twitchings of the muscles are common, especially in adult cases.

Perverse Movements.

Under this heading must be classed the very constant maladroitness of movement present in these cases, the facial overaction and grimacing in speech and in mimetic expression; choreic movements and athetotic movements and intention tremor. These forms of perverse movements are only present where the rigidity is slight. Athetotic movements sometimes are present in the face; choreic movements never. Not rarely choreic or athetotic movements are present in the upper extremities associated with slight rigidity, while severe rigidity affects the lower limbs.

Choreic movements may develop *pari passu* with the rigidity. A case of generalised rigidity may clear up for the most part leaving a choreic diplegia (Rosenthal). Athetotic movements always appear at a later date than rigidity. Cases presenting either choreic or athetotic movements are said never to improve after such movements have made their appearance.

Tremor precisely resembling that seen in disseminate sclerosis is sometimes seen in limbs where the rigidity is slight. Freud is of opinion that the so-called cases of disseminate sclerosis in children are in reality cases of diplegia. A case recently under the care of Dr. Hughlings Jackson at the National Hospital is interesting in this connection. A girl, after a severe attack of pneumonia at 7 years of age, slowly developed symptoms. On examination two years later she presented mental dulness, marked nystagmus, slight convergent strabismus, pallor of both optic discs, an expressionless face with slowness of articulation, marked intention tremor of the hands and spastic paraplegia, with slight rigidity of the upper limbs and increase of all the deep reflexes. The case presented as one of disseminate sclerosis. The symptoms agree equally well with the diagnosis of cerebral diplegia, and in addition to the above-mentioned signs this patient presented marked arrest of growth of the left side of the body,—face, arm and leg.

Common sensation and the muscular sense are unimpaired in the cases where their accurate investigation is possible.

In the severe cases there is very great pain on passive flexion of the rigid joints probably owing to the formation of rest adhesions.

Trophic changes are confined to a stunting of growth, but this is not nearly so well marked in the diplegias as in infantile hemiplegia and in bilateral spastic hemiplegia. In diplegia the bilaterality of the distribution renders it difficult to estimate.

The sphincters are unaffected.

The deep reflexes are exaggerated, but are difficult to obtain in limbs which are very rigid, and for this reason foot clonus is not generally obtained. Of the superficial reflexes those of the trunk are absent in marked cases. The plantar reflexes have, in the cases under my observation, always shown an extensor response, and in a recent communication I have laid stress on the connection between this form of plantar reflex and the presence of pes cavus.

With the class of cerebral diplegia just described I would include the very characteristic group of cases brought into notice by Waren Tay, B. Sachs, Hirsch, Peterson, Kingdon and others, and recently described in detail by Kingdon and Risien Russell in "Allbutt's System of Medicine" under the title of "Infantile Cerebral Degeneration." The symptoms of this disease are those of generalised rigidity, and but for the retinal change could not be distinguished. The same morbid changes which have been found constant in this disease have been found in recent cases of generalised rigidity; in two cases here recorded by Risien Russell, by Mya and Levi, by Warda, and by Sachs.

In the reported cases of this type the patients have all been Hebrews. The disease is familial. There have been no known clinical antecedents. Birth has always been natural and at full term. The patients are healthy up till between the third and sixth month when general weakness comes on insidiously, and is followed some little time later, if the child live, by generalised rigidity associated with muscular wasting. Great mental failure, optic atrophy, and peculiar retinal changes (*vide ante*) are present with the usual signs of generalised rigidity. This disease has proved fatal in all cases at an early period, generally before the second year of life.

Atypical Forms.

(*Formes frustes de rigidité generalisée, Rosenthal.*)

These cases are placed under a special heading because of their peculiar clinical aspect. They present slight symptoms of generalised rigidity with profound mental changes, which generally amount to complete idiocy. Rosenthal has suggested that in these cases the incidence of the cortical lesion is chiefly upon the frontal convolutions.

Bilateral spastic Hemiplegia.

Severe forms of this condition cannot be distinguished from the most severe cases of generalised rigidity, as the distinguishing symptom—the paralysis and its distribution—are in both conditions absolute and general. In slighter forms the type is characterised by the preponderance of paralysis over the rigidity, and by the fact that in these cases the arms suffer more than the legs as in the common type of hemiplegia. Stunting of the growth of the limbs is much more marked than in the other forms of diplegia. The occurrence of convulsions is common, and occurs in 44 per cent. of the cases (Sachs, Gaudard, Wallenberg). The majority of the cases are congenital. The pathological distinction between bilateral spastic hemiplegia and generalised rigidity is that in the former case deep lesions of the hemisphere, and in the latter case superficial lesions, are found.

Paraplegic Rigidity. (Rigidité Paraplégique, Freud. Paraplégie spinale spasmodique, Erb. Little's disease, van Gehuchten.)

In this type the rigidity and paresis are confined to the lower extremities. Tardigrade progression, or the cross-legged progression, or the "broken-backed" progression is present. Adductor and extensor spasm of the legs with pes cavus is the rule. Not rarely there is hyper-extension of the knees. The general description given in the description of generalised rigidity applies, as regards the lower extremities, to this type.

Convergent strabismus occurs more frequently in this type than in the others, and is found in 30 per cent. of the cases (Freud).

Mental defects, difficulties of speech and of swallowing occur as frequently as in the other types, but for the most part in a lesser degree of severity, though this is not always the case.

Convulsions are present in 36 per cent. of the cases (Sachs, Osler, Wallenburg, Gaudard).

Combinations of paraplegic rigidity, with choreic diplegia and with bilateral athetosis, occur.

Bilateral Athetosis and Choreic Diplegia (Congenital Chorea).

The essential feature of the types consists in the presence of constantly occurring spontaneous movements which may affect all the muscles of the body. Bilateral athetosis and choreic diplegia are only separated as types by the form and extent of the spontaneous movements, and the two forms of movement may occur in the same case.

The movements of athetosis are slow, rhythmical, and affect the peripheral parts of the limbs most.

The choreic movements are quick, shock-like, localised, and affect the proximal parts of the limbs most. The term "choreic movements" is an unfortunate one, as the movements in no way resemble those of true chorea. They resemble closely the movements of myoclonus and the description of the movements in Dubini's disease.

Choreic movements are hardly ever seen in the face, but in two brothers affected with choreic diplegia recently observed at the National Hospital such movements constantly occurred in the tongue and palate. The movements in these cases showed violent exacerbations, and during periods of increase the movements were always present in the facial muscles about the angle of the mouth. The laryngeal muscles were not affected.

The trunk muscles are often affected.

Choreic movements always cease during sleep.

Athetosis frequently affects the face, and is associated with great facial overaction and grimacing on voluntary movement. The tongue when at rest in the mouth and when protruded may show most evident athetosis. In severe cases all the muscles of the body may be affected, and the movements beginning in one limb may spread successively to the other limb on the same side, and then to the opposite limbs. In some cases the movements are confined to one region of the body. The face or the upper or lower extremities may be affected alone. Athetotic movements sometimes continue during sleep. Slight generalised rigidity and paresis are present in these cases, though they may amount to little more than an increase of the deep reflexes and slowness of voluntary movement. The same mental changes, affection of speech, nystagmus, strabismus, optic atrophy, and dysphagia as have been described in "generalised rigidity" occur in bilateral athetosis and in choreic diplegia. A few points, however, demand special notice. Even in the most severe cases of bilateral athetosis the mental changes may be very slight. Convulsions are common in choreic diplegia, but are very rare in cases of bilateral athetosis. In both types intention tremor is not infrequently noticed. In athetosis actual hypertrophy of the muscles is sometimes seen.

Course of the Disease is Cerebral Diplegia.

Some cases are regularly progressive either rapidly or slowly, and this generally is the case with the more severe forms of generalised rigidity. Others after the symptoms have reached a certain degree of intensity may remain stationary or may tend to improve. The latter result is more often seen in cases of paraplegic rigidity and slight generalised rigidity. The amount of improvement is, however, rarely great. In slight cases of generalised rigidity the symptoms may disappear from the upper limbs, leaving a condition of paraplegic rigidity. Osler has noticed slight cases in which all the symptoms have disappeared except epilepsy; van Gehuchten states that cases of paraplegic rigidity regularly tend to improve. Most writers, however, agree that improvement takes place only to the extent of gaining some poor power of walking, and that this much occurs only in some cases.

Bilateral hemiplegia is always stationary.

Improvement is, perhaps, never met with in bilateral athetosis, and choreic diplegia and cases of athetosis are usually progressive.

Speaking generally, cerebral diplegia tends to shorten life much more than does hemiplegia, and few infantile cases reach adult life.

The Morbid Anatomy and Pathology of Cerebral Diplegia.

The pathology of this disease has been the subject of much controversy, and the most diverse opinions have been and are still held concerning it.

Though a considerable number of autopsies are recorded, deductions as to the nature of the morbid process have been beset with great difficulties. In the majority of the reported cases the examination has been made long after the onset of the disease, and from the final lesions found it has been impossible to infer with certainty the initial lesion. Only a few autopsies have been performed at a time when the initial lesion can be said to have been recent. It is only recently that the tissues have been examined by the new methods of histological examination. Further difficulties arise from the fact that the final changes found are not constant, and that the same final changes have been proved to be produced by different initial processes. Moreover, the final lesions described have not been sufficient in some cases to explain the symptoms. In two cases similar in origin, course, and symptomatology, widely different final lesions may be found; as for example in the cases reported by Otto and Warda. It has been impossible to foretell from the clinical aspect of a case what lesions would be found, nor has it been possible to deduce the clinical type of the case from the final lesions found. It has been stated by Freud that the symptomatology is determined by other than the anatomical conditions so far brought to light in these cases. Too much stress has been laid perhaps upon the coarse anatomical lesions which may be only secondary results of primary degeneration in the nerve elements themselves, and these last factors alone may determine the symptomatology. To this conclusion the results of recent investigations, especially upon cases examined soon after the disease has set in, tend.

Certain anatomical conditions, which are found as final lesions in cerebral diplegia, seem to be peculiar to the infantile brain; they are the conditions described here as diffuse and lobar atrophy of the convolutions and porencephaly. Freud has suggested that lesions which in the adult brain produce softening, cicatrisation and cysts, produce atrophic sclerosis and porencephaly, on account of the greater vitality of the glial tissue, which remains alive after evascularisation in the infantile brain.

Final Lesions found in the Cerebrum.

(i.) *Diffuse Lobar and Partial Atrophic Sclerosis.*—In this condition, which is found alone in 50 per cent. of all cases (Osler, Richardiere), 84 per cent. (Sachs), there is atrophy of the convolutions without disturbance of their form or arrangement. It may affect the whole cortex or may be confined to certain regions. The atrophy is often symmetrical. The weight of the hemispheres is lessened, and the consistence of the brain substance increased. The cerebellum may be uncovered. The atrophy is always found to affect the Rolandic convolutions more or less, and has a special preference for the occipital lobe in many cases (Richardiere). In connection with atrophy of the hemispheres, there may be marked atrophy of the cerebellum.

The meninges are never affected.

The convolutions are small, and the sulci are widened. The cortex is thinned, and its surface often presents a worm-eaten appearance. The white matter of the centrum semi-ovale is reduced in size, and is of a deep greyish colour. The ventricles are often enlarged. Occasionally "plaques jaunes" and small cysts are found in connection with the atrophy.

Microscopically, the condition of the grey matter is one of increase of the glial tissue, with thickening round the blood-vessels, and atrophy or disappearance of the nerve elements.

In cases where the examination has been made soon after the onset of the disease, the atrophy of the convolutions has been much less marked. The increase of glial tissue has been less marked, and in some cases absent. The atrophy of the nerve elements has been conspicuous.

Under this heading come the autopsies recorded by MacNutt, Railton, Marie, Jendrassik, Warda, Mya and Levi, Sachs, Cotard, Schultze, Anton, Money, Henoch, Förster, Isambert, Bechterew, Russell, Robin, Friedmann, Muratoff, Schmaus, Gee, Richardiere, Bourneville and Brissaud, Dejerine and Sollier.

(ii.) *Patchy Sclerosis.*—This condition described by Bourneville differs only from the preceding in that the atrophy in each convolution was local, producing a knobbed appearance, the convolution being alternately shrunken and hypertrophied, the projecting portions showing great increase of the glial tissue ("sclerose hypertrophique").

(iii.) *Porencephaly.*—This term was first used by Heschl for large and localised defects of the cerebral substance leading to a thinning or absence of the wall of the lateral ventricle.

Such porencephalic defects may occur in any part of the hemisphere, but they are more common in the Rolandic region; they are very often symmetrical. In two-thirds of von Kahlden's cases the defect was bilateral and symmetrical. The following forms of porencephalic defects are described:—(1) The cavity, crossed by trabeculæ, forms a spongy mass communicating neither with the ventricle nor with the sub-arachnoid space. Rarely the condition is one of multiple cysts. (2) The defect takes the form of a space communicating with the ventricle. (3) There is a complete absence of the wall of the lateral ventricle at one spot, the ventricle and subarachnoid space communicating. The hemisphere may be reduced for the most part to a thin-walled cyst, when a large defect of the second variety is present. The wall of the cavity is smooth, and is not fibrosed. Pigment has been found in the wall in one case, and from this fact an origin in hæmorrhage was argued. The convolutions in the neighbourhood of the porencephaly are small and sclerosed as a rule. The convolutions either are normally arranged and are cut off sharply at the edge of the defect, as if this had been punched out, or they radiate towards the defect, as do the spokes of a cartwheel to its centre, becoming smaller towards the edge of the porencephaly, and gradually sinking into it. Kundrat considered that the arrangement of the convolutions in the neighbourhood of the porencephaly was conclusive proof as to its congenital or acquired origin, the variety with the cartwheel arrangement of gyri being congenital, the other acquired. This argument has proved incorrect, for undoubtedly congenital cases have been reported by Anton, Schultze, and von Limbeck, where the arrangement of convolutions has been normal; and, on the other hand, the radiate arrangement has been found in cases certainly post-natal by von Monakow, von Kahlden, and others, and has, with a condition of porencephaly, been produced experimentally in animals by Bikeles and D'Alundo.

In cases of diplegia, where the symptoms have been strictly symmetrical, unilateral porencephaly has been found, associated with microgyria and sclerosis of the convolutions of both hemispheres.

In the general or local atrophy of the convolutions associated with porencephaly, atrophy and disappearance of the nerve elements with sclerosis is always found. In one case the artery supplying the region of the defect was absent.

Autopsies have been recorded by Heschl, Kundrat, Herter, Böttger, v. Monakow, v. Kahlden, Bourneville, Dausiac, Heubner, Koenig, Ross, Otto, De Forest Willard, Mierzejewski, Muratoff, Petersen, Ganghofner, Schultze, Anton, v. Limbeck.

(iv.) *Hydrocephalus.*—Ganghofner brought this condition forward as the final lesion and cause in three cases of diplegia. In one of these cases the cortical grey matter is stated to have been much reduced. There was no report of histological examination.

(v.) *Chronic vertical lepto-meningitis.*—This condition is rarely found. Cases of diffuse atrophy of the cortex with thickening and adhesions of the pia mater have been reported by Marie and Bourneville.

Initial Lesions and Processes.

(1) *Arrest of development.*—This has been brought forward by several writers as the factor in certain cases of porencephaly, and while perhaps true for certain cases,

where the defect forms an opening between the lateral ventricle and the subarachnoid space, as for instance in the case recorded by Ross, it is not proved. Porencephaly is not associated with either a low developmental type or an unusual arrangement of the convolution, such as might be expected, were it due to congenital arrest of development simply. Such alteration in the convolutions as does occur in this condition has been found in cases undoubtedly of post-natal origin.

(2) *Vascular initial lesions.—Meningeal Hæmorrhage.*—The origin of cerebral diplegia in meningeal hæmorrhage has been supported by many writers, MacNutt, Gowers, Taylor, and others, and it is considered to produce the final lesion lobar sclerosis.

Meningeal hæmorrhage is commonly found in young children. Weyhe performed 957 autopsies upon children from a few days old, to six months old, and found signs of meningeal hæmorrhage in 122 of the cases, that is in 13 per cent., though none of these cases presented any sign of damage to the brain. In 122 autopsies upon children the subjects of congenital syphilis he found meningeal hæmorrhage in 23 cases or in 19 per cent. Similar results were obtained in congenital syphilitic patients by Mracek. It is interesting in this connection that Koenigstein, in 1881, found retinal hæmorrhages common in newly born healthy children, and especially common in children born prematurely. There are only two recorded autopsies of cases of cerebral diplegia which bear upon this question, those of MacNutt and Railton. The following is a brief abstract of MacNutt's case.

The mother had two children still-born and two died soon after birth. Labour difficult. Breech delivery. Small emaciated child. Symptoms noticed directly after birth. Clinical aspect, severe generalised rigidity. Death at two and a half years. Condition found: Symmetrical and severe lobar atrophy affecting paracentral lobule most; to a less extent the central convolutions, and the roots of the three frontal convolutions. Meninges normal. Cortex of affected area destitute of nerve elements, and at edge of atrophic region gradual disappearance of nerve cells.

Some sclerosis in deeper layers of atrophic cortex. Typical bilateral degeneration of the pyramidal tracts.

Railton's case gave a similar history and result, except that there was no degeneration of the pyramidal tracts.

Dr. MacNutt figured the meningeal hæmorrhage found *post-mortem* in a newly-born child suffering from right brachial monoplegia, occupying the same situation as the atrophy in her case of diplegia, and argued from that, that meningeal hæmorrhage had caused the atrophy. No trace of meningeal hæmorrhage was found in her case, and the explanation was that it had been completely absorbed. But in children up to nine months of age suffering with no diplegic symptoms Weyhe repeatedly found distinct remnants of meningeal hæmorrhage that had occurred at birth, with no sign of cortical atrophy. It is difficult to explain, moreover, why a meningeal hæmorrhage should remain localised to a certain region of the subarachnoid space, and there be efficient to produce complete cortical atrophy, while the commonly occurring meningeal hæmorrhage in the subtentorial region produces no symptoms (Franz Schultze). The very general symmetry of the lesions, and often their situation in cases of atrophy of the cortex, make the explanation of meningeal hæmorrhage, as the initial lesion producing diffuse and lobar cortical sclerosis, a very difficult one. That meningeal hæmorrhage is common in young children is proved, but that it can produce cortical atrophy and the symptoms of diplegia is not conclusively proved. Neither in MacNutt's nor in Railton's case can meningeal hæmorrhage be said to have occurred undoubtedly as the initial lesion.

Embolism.—The frequency of the affection of the central convolutions in cases of cerebral diplegia suggests as a cause interference with the blood supply to that region by the arteria centralis media. Abercrombie and Schultze are the chief upholders of the theory of embolism to account for lobar sclerosis. Freud in *La Nouvelle Iconographie de la Salpêtrière* reports a case of diffuse atrophy of the hemispheres undoubtedly the result of embolism. Delettre, Charcot, and Heubner have reported similar cases. Heubner, Schultze, and Krauser have each reported a case in which porencephaly resulted from post-natal embolism.

Diplegia is only in rare cases associated with pathological conditions in which embolism is likely to occur, and in this disease embolisms are rarely found in other organs. The likelihood of occurrence of bilateral symmetrical embolisms such as could produce diplegia, is small. Embolism, though perhaps a more common cause of hemiplegic infantile spastic states, cannot be considered as more than an occasional cause of diplegia.

Thrombosis.—Gowers advocates thrombosis of the cortical veins and of the superior longitudinal sinus as a cause of diplegia. In a case reported by Abercrombie diffuse atrophy of the convolutions with thrombosis of the superior longitudinal sinus and with widespread arterial disease was found: signs of congenital syphilis were present in this case. Angel Money found diffuse atrophy of the convolutions with nearly all the pia matral vessels thrombosed in a case of generalised rigidity. Cotard found obvious endarteritis associated with diffuse atrophy of the convolutions and "plaques jaunes" in one case. Kundrat considers many porencephalic defects to be the result of anæmic necrosis in fœtal life, probably the result of thrombosis.

In cases showing atrophy of convolutions and porencephaly, however, indications that those conditions were the result of thrombosis have only rarely been found, and in the cases examined soon after the onset of the disease to which the greatest importance must be attached, signs of thrombosis have been wanting.

Intra-cerebral hæmorrhage.—This initial process as a result of trauma at birth or in later life, and multiple hæmorrhage as a result of asphyxia neonatorum, have appeared likely from autopsies in which porencephaly was found by Herter, Bottger, von Monakow, and von Kahlden, and in the cases reported by the two last writers there had been severe injury produced by the forceps during delivery. In Ashby's case the condition of multiple cysts and sclerosis was attributed to multiple small hæmorrhages. Sachs and Petersen, speaking generally of infantile spastic states, consider cerebral hæmorrhage a common initial process. They came to the conclusion that of seventy-nine autopsies upon hemiplegic forms collected by them, twenty-three were due to intra-cerebral hæmorrhage, but they found no reason for considering it the initial process in twenty-five autopsies upon diplegic forms.

Inflammatory initial lesions.—Virchow in 1865 described a condition of "encephalitis congenitalis," and von Limbeck considered atrophic lobar sclerosis the result of this condition. Vizioli in 1880 advanced polio-encephalitis as a cause of infantile spastic states. Strumpell in 1885 brought forward cases of undoubted polio-encephalitis, and argued this initial process for infantile spastic states generally. The condition found in his cases was acute inflammation of the cortex with hæmorrhage. About the same time Wernicke brought to light similar cases, and in one case found this condition of encephalitis associated with polyneuritis and polio-myelitis affecting the anterior horn-cells of the cord and bulbar nuclei. The influenza epidemics brought many similar cases. Goldscheider, Eisenlohr, Leichtenstern, Bucklers, Friedmann, and Oppenheim, amongst many others, have recorded cases. This disease has occurred chiefly in adults; the initial symptoms have been very severe, and it is frequently immediately fatal. In cases that have survived the initial disease, the final lesion in cases examined has been very different to those found in cases of diplegia. Though a definite clinical entity, polio-encephalitis seems to have no connection with diplegia. Marie, however, inclines to the opinion that some cases of acquired diplegia with severe initial symptoms are of this nature. Strumpell considered both porencephaly and sclerosis the results of polio-encephalitis. His reference of polio-encephalitis and polio-myelitis to the same morbid agent has received no confirmation.

Degenerative initial lesions the result of toxic processes.—The majority of the known ætiological antecedents of cerebral diplegia, both congenital and acquired, are conditions suggesting the presence of a toxic state. In diseases of the nervous system, the result of toxic processes, the nervous elements usually suffer rather than the interstitial tissue. In familial nervous diseases, into which class diplegia comes to a considerable extent, it is natural to look to the neuron as the probable seat of initial disease.

Jendrassik and Marie strongly support the toxic origin of infantile spastic states. They consider that the initial process in cortical sclerosis is a sclerosis round the smaller blood vessels, the result of an infective toxic process.

In reported cases of atrophic lobar and diffuse sclerosis and in the sclerosis associated with porencephaly, marked degeneration or disappearance of the neurons of the cortex has been found. It has been argued that this sclerosis is a secondary sclerotic process, spreading from the site of a vascular lesion (cyst, bruise, "plaque jaune" or porencephaly), or it is occasioned by meningeal hæmorrhage, and that the destruction of nerve cells is secondary to the sclerosis (Schmaus).

Cotard, in 1868, first drew attention to an atrophy of the pyramidal neurons out of proportion to the sclerosis. Warda, in 1895, in a recent case of generalised rigidity with diffuse cortical atrophy, found disappearance and degeneration of the cortical neurons, and this was certainly not secondary to any sclerosis. Mya and Levi, in 1896, found the microscopic anatomy of the diffuse atrophy in a case of generalised rigidity to be arrest of development, and degeneration of the cortical nerve cells. Sachs, in a case which he had attributed to meningeal hæmorrhage, found a primary degeneration of the pyramidal neurons. In two of the cases reported in this paper Risien Russell found a progressive chronic degeneration of the cortical neurons, and the appearances suggested a toxic cause for this degeneration.

In all the cases of Waren Tay and Sachs type of generalised rigidity that have been examined, primary degeneration of the neurons of the cortex cerebri has been found. The atrophy of the convolutions and the gliosis has been shown in these cases to be secondary to the degeneration of the nerve elements, for in the cases when death occurred at an early period of the disease atrophy and convolutions and sclerosis were absent, or very slight, and in other cases the amount of atrophy and sclerosis were proportionate to the length of time the disease had lasted.

It has been already pointed out that the symptoms in cases of diplegia often do not correspond to the coarse anatomical lesions found. In a severe case of generalised rigidity reported by Ganghofner, no coarse lesion was found. This is easily explicable if the essential morbid process in such cases is a lesion of the neurons and the coarse anatomical changes are secondary to this.

It is then certain that the conditions—lobar and diffuse atrophic sclerosis—in some cases owe their origin to a degeneration of the neurons of the cortex. Some porencephalic defects and the associated atrophy of the convolutions may also possibly arise as secondary processes from the same initial lesion affecting the neurons.

Of all the pathological processes which have been brought forward as the primary causes of diplegia, degeneration of the neurons of the cerebral cortex is in most accordance with the clinical aspect of many cases of the disease. The association of the disease with toxic states of the mother and with premature birth; its post-natal origin after specific fevers and indefinite febrile attacks; its progressive course in many cases, and the variable mode of onset of the disease, are more compatible with this pathological explanation than with any other that has been brought forward.

The pathology of choreic diplegia.—While the lesions of brain found in this condition are similar to those found in the other types of diplegia, an attempt has been made to connect the presence of choreic movements with special lesions in the region of the corpora striata. Broadbent in 1869 found capillary embolisms in the corpora striata. Anton in a typical case of choreic diplegia found changes in the putamen, namely, sclerosis round the blood vessels and cicatrices which were probably the results of multiple softenings. In six cases Demange found changes in the lenticular nucleus. Such changes, however, are not constant. Probably choreic and athetotic movements are to be connected with superficial lesions of the cortex (Wallenberg, Freud). Such superficial lesions have been demonstrated by Kroemer, Kalischer, Kronthal, Oppenheim and Hope. The last two observers have found in cases of Huntington's chorea a condition which they described as miliary disseminate interstitial sclerosis of the cortex.

The condition of the pyramidal tracts in cerebral diplegia.—The following conditions have been found:—

(i.) Secondary degeneration of all the pyramidal tracts in the cord. This has been found in most of the acquired cases and in many cases dating from birth. When present it indicates that the onset of the disease occurred after the pyramidal tracts have been developed.

(ii.) Absence of the pyramidal tracts on both sides was found by Anton, by Schultze, and by Dejerine, and on one side by von Monakow. This condition suggests that the onset of the disease occurred before the development of the pyramidal fibres, and that the cortical neurons from which these fibres grow were so damaged by the morbid process that no development of these tracts could take place.

Freud states that in secondary degeneration the fibres of the pyramidal system may after a long time disappear so completely as to leave no trace of their existence. This may account for the absence of the tracts in some cases; possibly this had happened in Dejerine's case.

(iii.) Diminution of the size of the pyramidal tracts has been found by Osler and Ganghofner. A lesion of part of the motor cortex at an early date preventing the development of some of the fibres of the tract probably explains this condition.

(iv.) The pyramidal tracts may be normal. This condition has been found by Ganghofner and by Railton. (The method of examination is not stated.)

Further Pathological Considerations.

In diplegia the brain is usually affected during its development, and at this time there is more capacity for the repair of damage and for compensation than when the organ is fully developed. From this it may be said that the infantile brain is better protected against local lesions, but not so well protected against diffuse lesions, on account of the tissue instability, than is the adult brain.

Gowers, Anton and Freud have given a general explanation of the rigidity in diplegia as being the result of the isolation of the lower centres from the control of the cerebrum and the unopposed action of these centres. Rigidity does not depend upon any degeneration of the pyramidal tracts.

It has been pointed out by Freud that in newly-born infants, slight rigidity, and movements which call to mind both athetotic and choreic movements, occur normally.

Freud, Rosenthal and others investigating the connection of the rigidity and the paralysis in diplegia have come to the conclusion that in cases in which rigidity preponderates the cerebral lesion is superficial, and where paralysis preponderates the cerebral lesion extends deeply into the hemisphere.

A lesion extending deeply isolates the lower centres associated with the damaged region much more completely than does a partial lesion of the cortex.

In this connection a most interesting case is reported by Freud of generalised rigidity associated with complete left hemiplegia. Diffuse cortical sclerosis was found in both hemispheres, but in the corona radiata of the right hemisphere a cyst was found beneath the central convolution.

In the reported autopsies upon cases of bilateral spastic hemiplegia the lesions have either extended deeply or have completely destroyed the cortex.

There are several diseases of which the pathology is little known, which must be considered as closely allied to the cerebral diplegias. The two following diseases perhaps stand in very close pathological relationship.

(1) Adult familial paraplegic paralysis which has been described by Osler, Franz Schultze, Kraft-Ebing, Souques, Neumark, Erb, Melotte, Castellamessa, Koschewnikoff, Massolongo and Oppenheim.

(2) Forms of chronic spastic paralysis occurring in adults

often associated with mental changes. These conditions have been described by Pelitzoeus, Dreschfield, Freud, Higier, Friedmann, von Homen, Bouchard and Hoffmann, Bruns and Seeligmuller.

Showing a distant relation with diplegia are the diseases Huntington's chorea, Friedreich's ataxy, Marie's ataxy and myopathy, and certain facts showing this relation have been pointed out by Koenig, Strumpell, Bernhardt and Franz Schultze.

Summary of Conclusions as to the Pathology of Diplegia.

I. The cerebral lesions found in nearly all cases of diplegia are (1) atrophy of the convolutions; (2) porencephaly; (3) no coarse lesion but degeneration and disappearance of the cortical neurons.

II. The initial morbid process producing diffuse and lobar atrophic sclerosis are (1) degeneration of the neurons of the cerebral cortex; (2) vascular lesions, embolism, thrombosis and intra-cerebral hæmorrhage; (3) perhaps meningeal hæmorrhage.

III. Porencephaly may be produced by (1) arrest of development with tissue absorption owing to fœtal vascular disease; (2) direct injury to the brain; (3) vascular lesions after birth; embolism, thrombosis, and intra-cerebral hæmorrhage; (4) it may also result from the process of tissue absorption and shrinking of the brain substance occurring in cerebral sclerosis, and may result as a secondary process in degeneration of the cortical neurons.

IV. Bilateral spastic hemiplegia is connected with deep lesions of the hemispheres. The other forms of diplegia are connected with superficial lesions of the hemispheres.

V. Athetotic and choreic diplegia are associated with superficial lesions of the cortex. In these types lesions of the corpora striata are not constant.

Differential Diagnosis.

The diseases most likely to be confounded with cerebral diplegia are Marie's hereditary ataxy, Friedrich's ataxy, disseminate sclerosis occurring in children and familial spastic paralysis.

Treatment.

Only the slighter forms of generalised and paraplegic rigidity afford any scope for treatment.

Careful mental training and the regular use of appropriate gymnastic exercises may do much to aid improvement.

Slow extension and the division of tendons in slight cases where contractures have occurred have produced encouraging results (Edlenburg, Hoffe, Le Bonnardieres, and Lebrun).

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REMARKS ON JACKSONIAN EPILEPSY ILLUSTRATED BY AN UNUSUAL CASE.

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THE case occurred in the wards of Sir William Tennant Gairdner, K.C.B., while I acted as his resident, and I have to thank Sir William for permission to publish the case, and for the interest he has taken in this paper.[1]

It is not my intention to give a critical description of Jacksonian epilepsy, on which so much has been written, but, in order to increase the interest of the case now reported, I shall discuss shortly some of the more important points in regard to the history, physiology, and pathology of this disease.

At the outset I may state that I have made free use of an admirable article by Rauzier which appeared in the January number of *La Semaine Médicale*, 1893, and which contains a valuable epitome of the literature of the subject up to that time (1).

Another review, likewise full of information, is written by Burlureaux in the *Dictionary of Medical Sciences.* Interest in the subject is also aroused by the perusal of individual cases described by such masters as Hughlings Jackson (2), Charcot (3), Ferrier (4), Dreschfeld (5), Ross (6), Gowers (7), Broadbent (8), and Byrom Bramwell (9). French writers have added largely to the literature of the subject, among whom may be mentioned Bravais (10), Fournier (11), Girard (12), Greffier (13), Pitres (14), Charcot et Pitres (15), and Bourneville (16).

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[1] I have also to thank Dr. Ferguson for a pathological report, and Dr. Fred Dittmar for making careful sections of the brain tissue for me. To Dr. Samuel Prior I am indebted for the accompanying photomicrographs of the cerebral cortex, and to Dr. Hutton for his report on patient's condition on last admission.

History.

The medical history of convulsions dates back to the earliest times, and cases were described when only one side of the body, and indeed where only individual members were affected, but then *post-mortem* examinations, I suppose, were never made, and consequently no definite relation existed in the minds of writers between the central nervous system and the convulsive storms that occurred at various parts of the body. From the beginning of this century on to the middle of it, many cases were reported where convulsions affected certain parts of the body, and where definite organic lesions existed in the form of tumours, cysts, thickened membranes, &c., in the opposite side of the brain from the convulsed side, and yet these authors, both from want of experimental proof, and also from want of scientific reasoning, did not group the facts together in such a way as to establish a connection between the lesion and the convulsive seizures which were so accurately described.

Abercrombie (17), for example, describes as a class certain cases "distinguished by convulsions without any affection of the senses," where, he says, the convulsions may be confined to one side of the body, and he notes that in one case "there was a tumour on the surface of the opposite hemisphere, and in another a portion of the opposite hemisphere was indurated." He then, in fact, described a typical case of what we now call Jacksonian epilepsy, although he probably considered the presence of the tumour and induration as an accidental coincidence, and not the essential cause of the paroxysmal storm. In the same way Burlureaux (18) tells us that Parent-Duchatelet, Demongeret, Papavoine, Andral, and others, described cases of unilateral convulsions commencing in the fingers and corresponding with lesions of the ascending frontal convolutions of the opposite side, but they were entirely unaware of the pathological significance of these lesions.

The various forms of unilateral convulsions were first discussed by Prichard in 1822, when he called them local convulsions. Bravais (19), in 1827, called the condition hemiplegic epilepsy, as he had frequently noted paralysis to be a sequel to the convulsion on the affected limb. Elliotson (20), in 1831, designated the disease partial epilepsy, where only a part of the body was convulsed, so as to distinguish it from idiopathic epilepsy, which was more general. This term is frequently used to-day.

In 1861, Hughlings Jackson discussed the disease in the most suggestive manner, and after careful investigation so clearly and accurately argued on the facts that he set on foot a train of investigation which culminated in the well-known researches of Fritsch, Hitzig, and Ferrier, on the localisation of the motor areas in the brain. From that date the disease has been happily called "Jacksonian Epilepsy."

This form of epilepsy has a still wider nomenclature, according as the symptoms differ somewhat from those usually described by Hughlings Jackson, and from the frequent association of certain pathological conditions which give rise to it.

Charcot called one form "a partial tonic epilepsy," where, dependent on an organic lesion in the motor area of the brain, a group of muscles were in a state of tonic contraction, rather than in convulsion. Another form he designated "vibratory epilepsy," where there was a constant shaking of the muscles affected during the tonic stage. A third variety he speaks of as "l'épilepsie partielle sensorielle," where a severe ophthalmic headache accompanies the convulsive seizure.

As syphilis is such a frequent cause of these convulsions it has been often called "syphilitic epilepsy." Numerous are the writers that have approached the subject from this standpoint, more notably Fournier (21), Charcot (22), Barbier (23), and Mallet (24). Lastly, it has been termed by some "apoplectiform epilepsy," because the patient, the subject of true Jacksonian epilepsy, had occasional apoplectiform seizures. True Jacksonian epilepsy and apoplectiform seizures have been known to alternate in some instances, when the disease has received the name of "congestive apoplexy."

Physiology.

Hughlings Jackson, in his numerous writings, discussed the physiology and pathology of unilateral convulsions. Although at first he was not fortified by the results of physiological inquiry, he was of opinion that convulsions and hemiplegia were closely allied, and that the latter was merely the result of a more severe interference with the motor tract of the cerebral nervous system. Moreover, he concluded that convulsions were mere symptoms—the result of an over-excitability of certain motor nerve-cells, and although he was unaware of the particular nervous centres that were involved, apart from the fact that he had frequently seen *post-mortem* certain brain lesions on the opposite side of the brain, which he considered the cause of the irritation of the neighbouring brain substance, he was confident that different kinds of convulsions, as regards the part first affected, depended on irritative lesions affecting different parts of the brain cortex. In his own words, "a spasm beginning on one side implies local changes in the central nervous system as surely as one-sided palsy does;" and, again, "I [Hughlings Jackson] assert that there must of necessity be some place where the nervous system is diseased, or the spasm determined by causes acting generally would not be local."

He considered that there were centres for the face, arm, and leg, and that these were irritated in a definite order, just as he had noted that convulsions occurred in a definite order. He accordingly considered three varieties of convulsions :—

(1) Those beginning in the hand.
(2) Those beginning in the face and tongue.
(3) Those beginning in the foot.

It was not astonishing, then, that scientific observers were eager to submit these views to the test of experiment.

In Germany, Hitzig and Fritsch, and in England Ferrier, at once entered the field. Ferrier, in particular, experimented on monkeys, and successfully localised certain motor areas in the cortex cerebri.

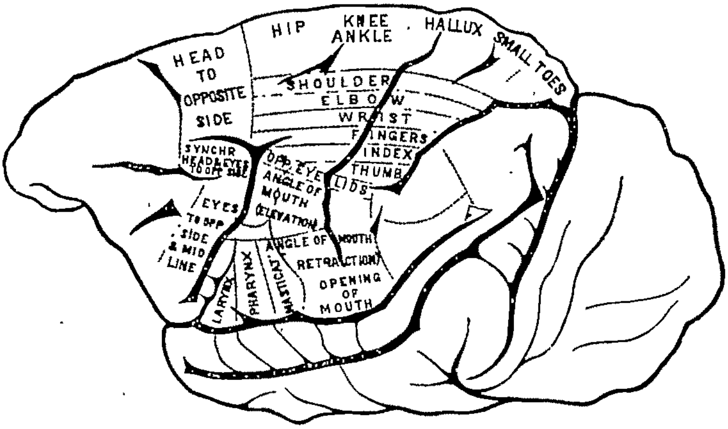
So indebted was he to Hughlings Jackson for the suggestion that led to this great research that he writes, "It is the great merit of Hughlings Jackson to have first clearly indicated the pathology of these affections" (convulsions) (25). His work on the "Functions of the Brain," published in 1876, Ferrier dedicated to Hughlings Jackson, "who from a clinical and pathological standpoint anticipated many of the more important results of recent experimental investigation into the functions of the cerebral hemispheres." A narrative by Ferrier, giving the experimental results, appears in the *Philosophical Transactions*, and at once there were two parties formed, the one side sceptical, the other full of belief.

Ferrier, however, was not the first to map out definite areas of the brain cortex that had to do with definite movements, for Fritsch and Hitzig (26) in 1870 discovered that the application of electrodes to an exposed part of the brain produced movements in certain parts of the body. There can be no doubt, however, that the results obtained by Ferrier were much more forcible and far-reaching than those of the German observers, and that they laid the basis of modern cerebral pathology, so far as motor areas are concerned.

The most notable of other writers who experimented in order to definitely localise particular cortical areas for definite movements were Beevor, Schäfer, Victor Horsley (27), Brown Sequard, Dupuy, and Burdon Sanderson.

For a time medical literature was teeming with the records of investigations by numerous experimentalists. When it was known definitely that particular areas in the cerebral cortex existed, which, when excited produced convulsions of particular muscles, and when destroyed caused paralysis without anæsthesia, clinicians and pathologists were ever on the look out for the discovery of brain lesions in the human subject that would correspond with definite symptoms observed during life. These efforts were richly rewarded.

We now know that the motor cortical area consists of a zone forming the convolutions around the fissure of Rolando, with pretty accurately defined areas for leg, body, arm, and face from above downwards. Irritation of these areas causes convulsions on the opposite side, and irritation of an area somewhat in advance of this causes deviation of the head and eyes to the opposite side (see diagram —Beevor and Horsley). Having discussed briefly the physiology of unilateral convulsions, I intend now to make a few remarks on their pathology.



Pathology.

What is the pathological lesion, and how does this lesion cause irritation of the brain cortex? It has frequently been called the "discharging lesion."

The pathological lesions may be divided into two classes:

(1) Those that can be seen by the naked eye. (2) Those that can be seen only by the highest powers of the microscope. It is probable that lesions may exist that cannot at present be seen at all, or demonstrated by any known method.

Of the first class, any form of tumour, cyst, thickened membrane, a blood extravasation in or around the neighbourhood of the fissure of Rolando, may cause convulsions, by irritation of the brain cortex.

This class practically includes all the forms of diseased brain tissue, meninges, and cranium in the region of the motor area of the brain. The various diseases have been enumerated by Rauzier (28), as follows:—

I. Affections of bone:—(*a*) tumours; (*b*) exostosis; (*c*) long splinter of bone.

II. Affections of meninges:—(*a*) tumours; (*b*) exudation, acute, subacute and chronic meningitis; (*c*) primitive hæmorrhages of meninges; (*d*) blood extravasations occurring in pachy-meningitis.

III. Affections of brain:—(*a*) Old and encapsulated abscesses; (*b*) cerebral sclerosis; (*c*) brain tumours; (*d*) hæmorrhagic foci; (*e*) ramollissement.

He lays special stress on traumatism and syphilis as causes in this form of unilateral convulsive seizure. An interesting table is appended by Rolland, who found that out of 112 cases forty-eight resulted from tumours, twenty-one from ramollissement, eight from traumatism, nine from superficial and deep aneurism, seven from cortical hæmorrhages, and five from cerebral atrophy.

The second class includes conditions in which there is possibly a change in the shape, size and number of the motor cells; or possibly from the help of modern histological methods of staining, a change may be detected in the protoplasmic substances of the brain cells; or the formation of a fatty substance around these cells; or possibly an interruption in the nerve fibres that proceed from these cells. There may be a minute change in the small arteries and veins that traverse the part—an arteriosclerosis. The origin or cause of these changed states of brain tissue is still obscure, but we must not overlook the fact that such minute changes in the motor area of the brain have been recognised with well-defined unilateral convulsions.

A greater puzzle in regard to the pathological significance occurs in certain cases where convulsions have been unilateral, and from a clinical standpoint entirely in harmony with the convulsions described by Hughlings Jackson, and yet have presented no cerebral changes that could be discovered even by the highest powers of the microscope. These cases have been described as functional, but on physiological grounds we may hold that where there are well-defined unilateral convulsions there is in all probability a local lesion. Possibly, however, the disturbance may be of a chemical nature.

We yet know but little of the chemical constitution of a nerve cell, or of the chemical phenomena happening in it. One can conceive that an altered metabolism, and an altered nutrition or change in chemical state or chemical process, may produce marked change in function.

Those belonging to the first class (including tumours, &c.), then, produce convulsions of the opposite side of the body by irritating the surrounding nerve-substance by their presence. It may be by pressure on the brain substance direct, or on the small vessels: or it may be by causing an inflammation. The surrounding cells are in a state of tension, and when this is sufficiently high there is what may be called a molecular explosion. This view is borne out by Hughlings Jackson and Charcot; and, moreover, they consider that the paralysis resulting is in consequence of the weakened and exhausted state of these motor cells after the explosion has taken place.

It is difficult to argue out the pathology of those belonging to the second class (with only microscopical changes, &c.), unless we uphold a chemical theory. Hughlings Jackson has expounded a view bearing on this subject which I will quote: "Speaking in chemical language, the highly unstable grey matter of disease remains of the same constitution as the comparatively stable grey matter of health, but that it is of a different composition; and a further speculation is that the phosphorous ingredient is replaced by its congener nitrogen—that the nervous matter is more nitrogenised, and therefore more explosive" (29). In support of this view it may be pointed out that artificial explosives like gun cotton, nitro glycerine, and prussic acid, always contain a loosely combined molecule of NO_2. The presence of the nitrogen molecule implies instability.

The actual convulsion is frequently set agoing by some peripheral irritation, or disease of the abdominal or thoracic organs. It may be that certain poisons are circulating in the blood, which either pick out the motor area and cause convulsions, or more probably by producing a pathological change in the brain tissue or its vessels. It is easy to understand how these poisons would produce convulsions by acting reflexly, provided that an organic lesion is already present; but if no such lesion exists, it is difficult to conceive of a poison picking out the motor area more especially, and consequently producing convulsions.

Still, writers have considered that poisons, such as alcohol (30), lead (31), and urea (32) in uræmia are capable of selecting one motor area, and of producing typical unilateral convulsions. They have called these "toxic epilepsies."

With these remarks on the history, physiology, and pathology of Jacksonian epilepsy, I shall now proceed to a description of a case, which I take to be one of this type of disease, although in many points it is not typical. I shall endeavour after its description to enter into a short discussion on its more important and interesting features.

E. McG., aged 38, a housewife, was admitted into the wards of the Western Infirmary on May 26, 1897, complaining of "fits."

History of Present Illness. Patient appears to have been free from any nervous disorder until a year ago, when, without warning, she fell down, lost consciousness, and remained for twenty minutes in what her friends called a fit. There was no return of "fits" until six months afterwards, when she again had an "attack" described by her friends as quite similar to the first. After this, the fits occurred pretty frequently, lasted from fifteen to twenty minutes, and in all of which she was totally unconscious. Three months ago, after one of these "attacks," she remained unconscious for five days, and during which time there occurred twenty fits (as informed by her friends), while, on regaining consciousness, she found there was considerable weakness of the right arm and leg.

She remained then free from the fits for six weeks, when a fit of a different kind developed, which recurred almost every ten minutes, and which, she says, corresponds almost entirely with those occurring at present. With these latter fits there is no loss of consciousness, but while it lasts, and indeed for some time afterwards, she loses the power of speech. Occasionally before the commencement of the fit she has a strange sensation in the throat. She notices that the head is drawn over to the right side, and that the arm and leg of the right side are thrown into violent jerking movements. They last only for one to two minutes. Apart from these fits she feels very well. The paresis which resulted some three months ago soon disappeared, and she can now walk perfectly and can use the right arm and hand as freely, she thinks, as the left.

She has never complained of ophthalmic headache, nor of any painful spot on any part of the cranium. Her digestion is good, and the bowels act regularly. She feels that she would sleep well if it were not for the "fits." Her eyesight is perfectly good. She has no abdominal pain, and no swelling of any part of the body. The urine is passed regularly, and she has not considered it unusual either in respect to its quantity or colour. During the fits she passes neither urine nor fæces into bed.

History of previous health. Patient has been a remarkably healthy woman, and apart from a pretty severe attack of rheumatism complicated with pleurisy, which occurred seven years ago, she does not remember having had a day's illness until the present trouble began.

Family history. There is a distinctly tubercular history manifested, as her father and sister, and apparently her mother also, died of phthisis pulmonalis. She has three brothers and three sisters alive and well. No history of insanity or nervous disorder of any kind.

Habits. She is married, but has had no children nor miscarriages. She denies having had any venereal disease, although she remarked that at one time her hair fell out very freely. There was no other indication, however, of any syphilitic taint.

Present condition. Patient is well nourished, and though somewhat pallid, to all appearances looks in ordinary health. There is no lack of adipose tissue, and the muscles are in no way atrophied or flabby. There is, however, a want of intellectual brightness in the eyes. The expression is dull and torpid, and she is slow in answering questions. There is no mental defect.

The pupils are equal, circular, slightly dilated, but respond correctly to light and in accommodation. The tongue is dry, and deeply fissured transversely—it is protruded in the middle line. Temperature is 97·8° Fah. Pulse is soft, easily compressible, and numbering 114 in the minute. There is no œdema of any part.

Heart is normal as regards percussion and ausculation.

Lungs are practically normal, although a few fine râles are heard at the bases, which accounts for a temporary cough and expectoration which at present exist. Nothing of note is discovered in the *Abdomen.* No movable or enlarged kidney; splenic and hepatic areas of dulness are within normal limits.

Urine is of average quantity, of a dark amber colour; acid reaction; faint mucous deposit; specific gravity 1022; no trace of either albumen, sugar, or blood; microscopical examination discovered a few mucous cells.

While the above report was being written, patient was seized with unilateral convulsions, which occurred almost every eight to ten minutes. They were all almost identical in their nature, they lasted from one and a half to two and a half minutes; commenced almost invariably with a twitching of the small muscles on the right side of the face (not entirely limited to this side however); there was then conjugate deviation of the eyes and face to the right side, shortly afterwards, but in some cases almost simultaneously with this deviation, a complicated movement of the right hand and arm commenced. All the fingers, except the first, are flexed at the metacarpo-phalangeal joints, while the terminal phalanges are in extension. The index finger thus assumes the pointing position. There is then a slight twisting movement at the wrist, the forearm is next slowly pronated and slightly flexed on the arm. During this period, patient frequently mutters to herself. The right leg becomes likewise slightly flexed at the knee joint.

This portion of the attack takes from twenty to thirty seconds when the clonic stage commences, *i.e.*, convulsions proper. There are twitchings of the muscles of the face to a slight extent, chiefly those of the mouth, but almost immediately there are clonic spasms of the muscles of the fingers and thumb of the right hand, then of the whole forearm and arm, so that the right upper limb is thrown into a series of irregular jerking movements. A few seconds after the onset of the convulsive seizure in the arm, the right leg gets convulsed, and is also thrown about in an irregular fashion. At first the convulsion affects the right side alone, but soon after the left arm is slightly affected.

The convulsive seizure commences quietly, but the movements gradually become more intense, reach a maximum, and then gradually subside.

The left arm, when affected in the attack, ceases to be convulsed first, then the right leg, then the arm, and finally the head and eyes rotate backwards into their normal position.

This description, I think, bears out pretty accurately what occurred, although in some fits there were slight modifications. For example, the movements of the arm seemed in some instances to precede the twitching of the muscles of the face, and conjugate deviation of the face and eyes to the right side. Still, I feel sure that in the majority of the fits, the face was first affected, then the arm; and finally the leg, although I have said that in some the arm appeared to be first affected, then the face, and lastly the leg.

The left arm, on occasions, did take part in the movements, but still, these were not of a convulsive nature, at least they did not correspond at all to those of the right.

The right arm was the part which, undoubtedly, took the greatest share in the convulsive seizure. She was perfectly conscious during the attack, but she could not speak. On occasions I asked her questions during the attack and she frequently said "yes," but this was the only word that could be got from her.

Two minutes after the cessation of the convulsive seizure she was able to talk quite distinctly and fluently, although slowly. During this attack the pupils dilated somewhat; the conjunctival reflex was never abolished; respiration and pulse rate increased in frequency; urine and fæces were not involuntarily evacuated.

She seemed to have no warning, other than a "gurgling sensation" in the throat. There was no scream, and no biting of the tongue or foaming at the mouth.

I could discover no paresis of the muscles of the face, arm, hand, leg or foot. Sensation was normal. Knee-jerks present, but not exaggerated. No pain on pressure of muscles, or along course of nerve trunks. No pain on palpation or percussion of the head.

The circumstances of interest were noted in the Journal from time to time, and I shall summarise them here.

May 27, 1897 (day after admission).—To-day, the day after her admission into hospital, patient informed me that she could not move her right arm or leg. She discovered this herself accidentally after one of the fits. The nurses said that the fits had just been of the usual kind, and had occurred every ten minutes on an average. I know that she never lost consciousness, but I am entirely unaware at what time the paralysis set in, and whether it was gradual or sudden. *The arm and leg lay helplessly by the side.* There was no loss of sensation, but she failed to distinguish the difference between the point of the finger and point of a pin on the right side. Apart from this paralytic condition of the right arm and leg, and to a slight extent of the right lower muscles of the face, she had no other unusual symptom. Speech was only affected during and immediately after the convulsions.

June 2 (seven days after admission).—Fits still persist almost as frequently as above noted. She can, however, now move the right foot slightly, although she fails at any attempt to move the right arm or hand.

June 9 (fourteen days after admission).—Since last note fits have gradually become less frequent. She has been taking large doses of bromide of potassium and the syrup of chloral hydrate.

Reactions to faradism, both as regards sensation and muscular contraction, are similar on the two sides.

The right leg can be moved with ease; the right arm not at all.

June 10 (fifteen days after admission).—A recurrence of fits, of a milder degree than those noted before, when the face and arm of the right side alone shared in the convulsive storm.

The right leg and left side of the body were in no way affected. The right hand and arm were undoubtedly the centres of the convulsive storm in each case, whereas the twitching of the muscles of the face and conjugate deviation of the head and eyes to the right side were less constantly present. The movements of the right arm and fingers of the right hand correspond entirely with the description given above.

The right arm and hand are completely paralysed; the right leg and foot can be readily moved. No anæsthesia, but *distinct analgesia of the right side of the body.*

June 12 (seventeen days after admission).—Since the 10th patient has had large doses of KI., KBr., and Am. Br., with the result that these milder fits above mentioned soon disappeared. She has had no fit since the night of the 10th.

The right leg has regained so much power that she to-day endeavoured to walk a little, with assistance, in the ward. She can now move the fingers of the right hand, and elevate the arm at the shoulder. *No albumen in the urine.* Patient feels very well.

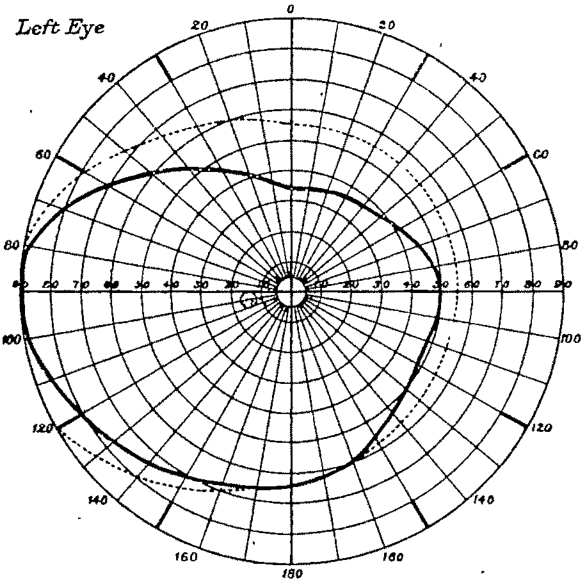
June 24 (twenty-nine days after admission).—Improvement has been steadily progressive. She walks in the ward every day, and the power of the right hand and arm is rapidly returning. No return of fits. Urine normal.

July 1 (thirty-six days after admission).—There is only a slight difference manifest in walking as regards the lower limbs, but it is evident that there is still a slight amount of analgesia of the right limbs. Tactile sensibility is normal.

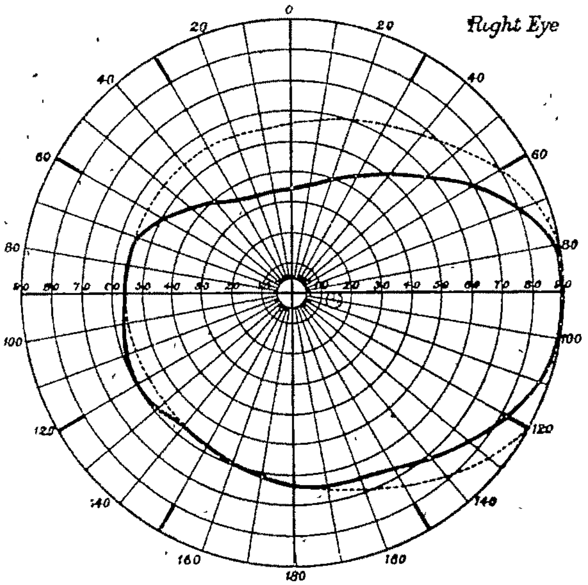
At the tip of the second finger in the two hands the distance by Weber's test is from ·3 to ·5 c.m. *Fundus of both eyes found to be normal.*

July 5 (forty days after admission).—Field of vision was tested to-day by means of the perimeter, and found practically correct on the two sides.

Chart of visual fields of both eyes :—



July 8 (forty-three days after admission).—To-day patient became sick, and she could not answer questions. On examination it was found that she failed to move the *left* arm. The right arm, which was originally paralysed, she moved quite readily.



July 9 (forty-four days after admission).—All signs of paresis of left arm gone.

July 10 (forty-five days after admission).—To-day there was a recurrence of the old fits—of exactly similar nature, but which lasted longer.

July 14 (forty-nine days after admission).—Patient has been menstruating for the last four days, and during which time she has had from eight to nine fits. On the 12th and 13th the fits resembled more the "Idiopathic" epileptic nature.

There was conjugate deviation of head and eyes to the right side, followed first by unilateral convulsions of the right side, which, however, soon after became general. The breathing was stertorous; the face livid; there was foaming at the mouth, and slight bleeding from the tongue and gums. She was quite well in from two to three minutes after coming out of the fit, and she had no drowsy stage, and no loss of control over the bladder and rectum.

July 23 (fifty-eight days after admission).—Patient has had no fits for over a week. Paralysis has almost gone, as she can walk perfectly, and perform the act of writing with apparent ease. *She was dismissed to-day well.*

August 6.—Patient had been advised to return to hospital during her next menstrual period, and so presented herself to-day. *Since last dismissal she has been well.*

August 10.—To-day with the right hand she turned the scale of the dynamometer to 35, and with the left to 55. She has had no fits, but she has been kept well under the action of the bromides.

Dismissed to-day well.

December 23, 1898.—*To-day, over sixteen months having elapsed since she was last dismissed from hospital,* patient was brought to the infirmary by her friends in a speechless and semi-unconscious condition.

The following history was given us by her friends:—It appears that from the time of her dismissal until yesterday, December 22, she remained to all appearance in perfect health, free from fits, and able to attend to her duties.

During this time she suffered neither from headaches, vomiting, pain after food, palpitation, breathlessness, dropsy of any part, pain in the abdomen, disorder of the bowels, retention or suppression of urine, or frequency of micturition; in fact, her friends state emphatically that she complained of nothing. Her appetite was good, and, indeed, as reported by Dr. Hutton, "might have been justly characterised as ravenous, particularly for nitrogenous food."

Although she appeared somewhat stupid on December 22, she took her dinner and supper heartily, and went to bed. She had had no shiver, or anything to have suggested the onset of an acute illness. At 2 a.m. on the morning of December 23 she was found to be in a fit, livid, and with "jerking movements of the right arm and leg, and snapping of the jaw." These convulsive seizures occurred very frequently, but her friends cannot say definitely how many she had. They were similar to those that occurred sixteen months ago. She was brought up to hospital at 6 p.m. on December 23.

A careful description of the fits was made at the bedside, and the following summary may be said to include all that occurred:—The convulsions were unilateral, confined to the right side, although in one fit the muscles of the face and arm of the left side appeared to participate in the spasm. The eyes first rotated to the right side, with nystagmus-like movements of the eyeballs; then the head rotated to the same side, with slight clonic movements, more especially of the levator labii superiors and zygomatics of the same side. The right arm was next affected, apparently in an almost identical manner to that fully described above, and lastly the right leg. Between the spasms she is apparently conscious, as she endeavours with the left hand to cover herself with the blankets. She cannot speak. The pupils are contracted, but equal. She is rather pale, but there is no puffiness of the face, although there is slight pitting on pressure over the tibiæ. No glandular enlargement.

Temperature is 101·4°, pulse soft, rapid, and numbering 142 per minute. Respirations are 32 in the minute. There is occasionally a period of respiration somewhat akin to the Cheyne-Stokes type. *There is a distinct paralysis of the muscles of the face on the right side, and complete paralysis of the muscles of the right arm and leg.* Plantar reflex is absent on the right side; knee-jerks are absent, and there is no ankle clonus.

There is complete anæsthesia of the right side of the body, and partial anæsthesia of the left arm. Heart and abdomen normal. Apart from a few rales at the extreme bases of the lungs (which were noted on last admission), these organs are likewise normal.

All the objective and subjective symptoms of the above report correspond pretty well with the report of her previous admission, but we have still to examine the urine, where we find proof of an acute affection of the kidneys. The first specimen examined contained albumen to the extent of ·1 per cent., urea 6 grs. to 1 oz. blood, a sediment which showed the presence of blood cells, epithelial tube casts, and uric acid crystals. The second specimen drawn off by catheter on the following morning, December 24, the day of her death, showed albumen to extent of ·9 per cent., a large quantity of blood, abundant epithelial, and other tube casts.

Hypodermic injections of pilocarpine were tried with only temporary benefit, and patient gradually passed into a condition resembling the "status epilepticus," and died at 3.50 p.m., December 24, 1898, after a two days' illness.

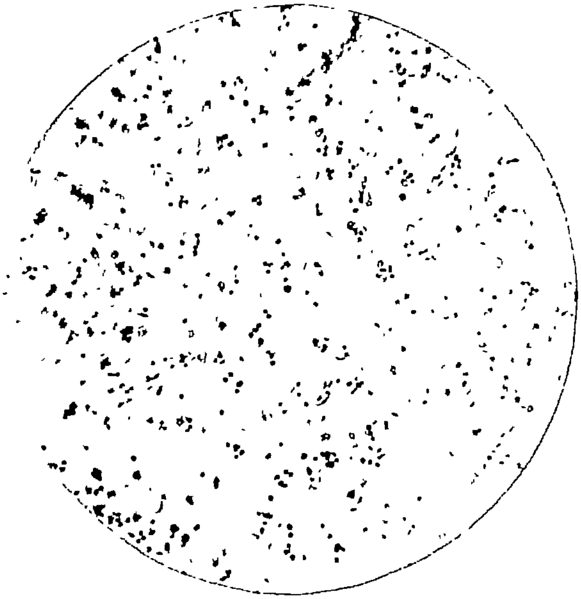
The temperature gradually rose after her admission, and shortly before her death it was recorded as 104° F.

A post-mortem examination was made, the results of which are briefly as follows :—

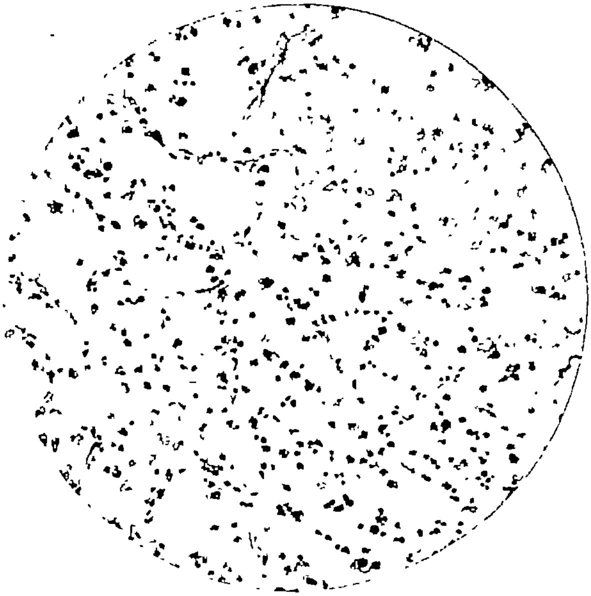
The heart is somewhat fatty, but there is no insufficiency of the valves.

The lungs are non-adherent, but considerably œdematous. Spleen and liver are large and soft with *post-mortem* staining. Stomach, intestines and pancreas are normal.

The brain is superficially congested posteriorly (*post mortem*). *Its substance shows nothing abnormal.* Dr. Dittmar in his report



Photomicrograph of section from left motor area.



Photomicrograph of section from right motor area.

says: "There is nothing unusual in the appearance of the microscopical sections which I have prepared from both motor areas of the brain—if anything there appears to be a preponderance of capillaries in that of the *right* side."

The kidneys present appearances of an acute cortical nephritis, accompanied by profuse desquamation and destruction of epithelium. The adrenals, ureters and bladder are normal.

I have described this case as fully as possible, in order that the various points of interest and difficulty with regard to its probable pathology and diagnosis may be criticised, and I shall now shortly discuss some of the problems that presented themselves under the headings of symptoms, diagnosis, ætiology and pathology.

SYMPTOMS.

Each fit was almost invariably ushered in by (1) *conjugate deviation of the eyes and head* to the right side. The axes of the eyeballs remained absolutely parallel. The movement was gradual, and free from any spasmodic jerking; moreover, there was definite precision in the commencement of rotation of both eyes and head. We know from the writings of Broadbent (33), Ross (34), and Gowers (35), how this symptom depends on some change in the opposite side of the brain, frequently produced by a hæmorrhage. If the muscles of the side opposite to the lesion are paralysed, then the antagonistic muscles draw both eyes and head to the non-paralysed side, *i.e.*, the head turns, and the eyes look towards the side of the lesion. However, if there is an irritation of one motor area, or rather of that portion of the cerebral cortex that has to do with the lateral deviation of the eyes and head, then the muscles of the side opposite to the lesion contract, and cause rotation of the eyes and head to the paralysed side, *i.e.*, the head turns away, and the eyes look from the lesion. In this case, there was probably an irritation of that area which lies immediately in front of the truly motor zone (see diagram of Beevor and Horsley), and, as a result, the nucleus of the sixth nerve of the right side was irritated, which produced contraction of the right external rectus, directly and indirectly, through the communicating fibres from this nucleus to the third nerve and spinal accessory of the opposite side, produced contraction of the left internal rectus, and left sterno-mastoid, although the right inferior oblique muscle (as described by Ross) also probably contracted. I consider that this area was the first to become irritated, and, owing to its physiological situation, this fact accounted for the convulsive seizures that depended on irritation of the neighbouring areas for the face and upper extremity. There was never any sign of paralysis of the orbital muscles, as is frequently the case from certain brain tumours.

(2) *Hemiplegia* occurred, not as is usually described by Hughlings Jackson, but in an irregular fashion, and with apparent suddenness. As we have above noted, hemiplegia after unilateral convulsions depends upon the weakened state of certain motor nerve cells after the explosion, which produced the convulsions, had taken place. One would expect to have a gradual hemiplegia resulting from a gradual exhaustibility of the motor cells due to frequent explosions of nerve energy. In this case we must consider the form of epilepsy as one of the apoplectiform or congestive type. The history obtained from patient's friends tells us of the suddenness of the onset of fits, the period of over a week's unconsciousness, the resulting hemiplegia of the right side of the body—on her admission we observed the occurrence of numerous fits with no evidences of hemiplegia, but, on the day following, the development of paralysis of the right arm and leg—and, again, on her last admission, we noted hemiplegia with paralysis of the lower muscles of the face on the right side.

It is not likely that in this case there were actual hæmorrhages in the cerebral cortex, as there would have been evidences *post mortem*. It is quite probable that after a more severe convulsive attack, the vessels in the neighbourhood of the left motor area became contracted, and a congestion resulted, allowing of a greater disturbance to the nutrition of these motor nerve cells.

It is difficult to account for the very fleeting paralysis of the left arm that occurred on one occasion, as this was preceded by no convulsive attack.

(3) *Aphasia* occurred shortly after the commencement of each fit, and lasted, as a rule, for two minutes after the cessation of the convulsive seizure. Aphasia, as has been graphically described by Hughlings Jackson, occurs almost invariably when the spasm begins in the right side of the body. In this case, the defect of speech was not due to difficulty of articulation, depending on paralysis of the labial muscles, but was from a true aphasia, the result of some change in the speech-producing centre on the left side of the brain.

Todd, in his lectures on Diseases of the Nervous System (lecture xv.), says:—"There is a peculiar class of cases of epileptic hemiplegia, in which the exciting cause of the epileptic fit at the same time damages or greatly injures voluntary power and speech." A factor in support of the view which I have expressed above, that the convulsive storm appeared almost invariably to start in the face, is the fact that Hughlings Jackson observed that aphasia frequently occurred when the face was first affected, but rarely when the convulsion commenced in the arm or leg.

An interesting case is reported by Sorel (36), where the symptoms were in many respects similar to the one at present under consideration. In Sorel's case the convulsions started in the face, but were preceded by conjugate deviation of the eyes and head. There was also *aphasia.* This transitory aphasia has been noted also by Audrey, Weber, Brown Sequard, and others.

(4) *Loss of consciousness* is rarely present in true Jacksonian epilepsy, and the victim of these convulsive seizures can, as a rule, describe accurately the general march of the storm, and repeat the various events that happened during the attack. Apart from her severe illness at the commencement of the disease, when her friends described her as unconscious for a week, and apart from her condition towards the end of her illness, which resembled the *status epilepticus,* she was perfectly conscious during all the convulsive seizures.

(5) *Disturbances of sensation* are rare accompaniments of Jacksonian epilepsy, whether there is post-epileptoid paralysis or not. I think one of the most important and interesting features of this case was the presence of analgesia of the right leg, and less markedly of the right arm, during most of her illness, and the complete anæsthesia of the whole right side of the arm and leg during the latter days of patient's life.

We know that anæsthesia does occur in some forms of Jacksonian epilepsy, depending on a syphilitic affection, but in these cases it is disseminated, occurring in patches over the backs of the hands, and perhaps outer aspects of the leg (Fournier, Barbier). But, in this case, we had no definite history of syphilis, and certainly *post mortem* there were no changes at all suggesting such a condition.

The question of anæsthesia and analgesia in relation to cerebral localisation has been put to experimental test by Ferrier, Schäfer, Horsley, and Yeo. All experiments show that destruction of the motor areas of the brain, however extensive, does *not* produce either anæsthesia or analgesia. These observers have found that the cerebral centres for such sensations lie in the hippocampal and inferior temporal regions, and also in the gyrus fornicatus.

I consider that in this case, the presence of analgesia, and anæsthesia shortly before death, depended most probably on certain changes that had taken place in the communicating fibres that connected the tactile centres with those of the motor region. Few cases are recorded where anæsthesia was present with unilateral convulsions, but one described by Broadbent (37) is of great interest. He records a case of epileptoid convulsions with hemi-anæsthesia, and in discussing the case, he says:—"Another very interesting feature in the case was the loss of sensation, which for a time was absolute in the right hand and arm, and well marked, though not complete in the body and leg of the same side." As this patient was cured under large doses of iodide of potassium, it is possible that this case belonged to the syphilitic group, where convulsions and anæsthesia have been frequently recorded.

DIAGNOSIS.

Whenever convulsions are unilateral, occurring seldom, and it may be in rapid succession, where definite parts of the body are affected, and where the convulsive storm is ushered in by the contraction of a particular group of muscles, with no loss of consciousness, at any rate at the commencement of the spasm, then we are dealing with a case of Jacksonian epilepsy. It matters little what the cause may be. The essential feature in such cases is the fact that a particular motor area, or only a portion of it, is irritated. So that, if in hysteria, when we speak of a functional state, definite unilateral convulsions exist, the case is one of Jacksonian epilepsy, provided that the seizures are not feigned.

Again, if in uræmia the convulsions are unilateral and consequently depend on irritation of the motor area by urinary elements, the same diagnosis may be arrived at. The two sets of cases might be talked of as hysterical and uræmic convulsions, assuming the Jacksonian type.

Still, other symptoms being taken into account, we are able to distinguish the disease from others, more especially from hysteria, true epilepsy, hystero-epilepsy, and uræmia.

(*a*) *Hysteria.*—In very few respects did our patient's condition present the characters of the "hysterical attack."

There was no emotional utterance before the seizure—no sudden falling to the ground with feigned loss of consciousness—no subsequent coma and fits of laughing and crying. There was no drooping of the eyelids. There was, however, hemiplegia and sensory disturbance, affections which are frequently present in hysterical patients, but in such cases one never meets with convulsions which pursue an almost exact course in each seizure, as in the present case.

(*b*) *True epilepsy.*—Although at one time the fits more closely resembled the truly epileptic nature, as a rule they largely differed from them. There was no history of epilepsy or other neurotic disease in the family—patient had had no convulsions or fits as a child—unconsciousness practically never existed—there was rarely biting of the tongue, and at no time was there loss of control over the bladder and rectum. Moreover, the fits were localised, and were almost invariably unilateral. On one or two occasions, due to the severity of the storm, the left arm participated in the attact, but the fits may be definitely said to have never been general, In four minutes or so after the seizure she was well.

(c) *Hystero-epilepsy.*—Charcot (38) in one of his lectures describes this disease as one of a truly hysterical nature, but which assumes, owing to the severity of the hysteria, an epileptoid condition. He entirely dismisses the theories that have been suggested of an admixture of the two diseases, hysteria and epilepsy. If this be correct, then we are at a loss as to the cause of the irritation that produces the epileptoid attacks.

In hysterical patients there may be a "*functional neurosis,*" but this functional neurosis implies, on physiological grounds, change (it may be temporary) of nerve elements. However, in hystero-epilepsy, the convulsions correspond to the idiopathic epileptic type, and are not localised as in Jacksonian epilepsy.

Besides, there is, as a rule the hysterical crying at the commencement of, and the cataleptic state after, the convulsion. Although we are not aware of the change that occurs in the brain as a result of hysteria, it is quite within the range of possibility that hysteria, which may assume the truly epileptic nature by disturbance of the whole cerebrum, may as readily assume the Jacksonian type by irritating one motor area. Such a disease might well be called *Hystero-Jacksonian epilepsy.*

By this term, however, I intend to denote hysteria as the primary disease with, as a sequel, irritation of one motor area from some nerve change, the cause of which is as yet unfathomed. At the same time, I fail to see why one motor area could be so isolated.

It is easy to distinguish Jacksonian epilepsy from the hystero-epilepsy of Charcot, but when we endeavour to distinguish it from the disease which I have designated as hystero-Jacksonian epilepsy, it is more difficult, especially when we consider certain points in the history, and symptoms of our patient, and the absence of any macroscopic or microscopic change in the motor zone.

I do not, however, uphold the idea of hysteria as the essential disease in this case; but whether hysteria be an element in the case or not, it matters little, for the disease is one of Jacksonian epilepsy, whatever be the cause.

(*d*) *Uræmia.*—We are aware that in certain forms of Bright's disease, the first symptoms are ushered in by convulsions. They may be epileptic in character, and indeed well localised and unilateral (39).

Had the disease in the present case depended on a chronic nephritis, no symptoms of which had presented themselves when the convulsions began, there would almost assuredly have been the development of symptoms during the long interval that elapsed between her second and last admission into hospital. Although the convulsions in uræmia at times do resemble Jacksonian epilepsy, and although French writers discuss a toxic epilepsy depending on the action of the urinary elements on one motor area, as a rule the convulsious are less accurately defined, and do not pursue the course that has been described.

The only place that we can give to uræmia is in the latter stages of patient's life, when an acute nephritis developed, these urinary elements acting on the already changed or susceptible motor area of the brain.

ÆTIOLOGY AND PATHOLOGY.

Had there been any macroscopical or even microscopical change in the left motor area of the cerebrum, it would have been an easy matter to discuss the ætiology and pathology of this case. The accompanying photomicrographs and report by Dr. Dittmar on the histological appearances negative any such change. For this reason the case is all the more interesting, even though any theories or views that may be advanced are speculative.

That the left motor area of the brain was irritated, and at certain times excessively so, is a fact that must be accepted.

The symptoms that presented themselves were in all respects in harmony with our knowledge of unilateral convulsions depending on an irritation starting at a definite point in the motor area, and spreading from that region to the parts around in definite order. The irritation started in the area for lateral deviation of the eyes and head, passed across to the centre for the face, interfering with the communicating fibres that had to do with tactile sensibility and the speech-producing centre, then passed up the fissure of Rolando to the centre for the arm, and then for the leg.

As there was no tumour, change in walls of arteries, cicatrisation, or evidence of ramollissement present, we must fall back on one of two theories as the cause of the convulsive seizures, the one vaso-motor, the other chemical. The first of these would account for the apoplectiform nature of certain of the fits, due probably to a contraction of some of the smaller arteries producing a congestion of the surrounding neuroglia; this might cause effusion which disappeared again by absorption, and left no trace *post mortem.*

The other theory, chemical in nature, has been already described in the remarks at the commencement of this paper on the general pathology of Jacksonian epilepsy. Either of these theories is possibly correct, and yet it is difficult to conceive why in both instances there should be vaso-motor and chemical disturbances in so localised an area.

Granted then that from either of these causes, or possibly from some other, the left motor zone, or part of it, is changed in nervous structure, or rendered susceptible, it is easy to understand the remaining difficulties that presented themselves. The convulsions ceased after a time, and were set agoing by the next menstrual period. This then might be an exciting cause which acted reflexly on the previously changed or susceptible area.

We might possibly have a *reflex Jacksonian epilepsy* in this instance. But after over a year's cessation of the fits, and owing to the occurrence of an acute nephritis and the absorption of urinary elements into the blood, *a toxic Jacksonian epilepsy* occurred, depending on the action of these elements on the old standing susceptible left motor area of the brain.

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A CASE OF NARCOLEPSY.

BY JOHN McGEE MACCORMAC, M.D.

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As classical cases of narcolepsy are rare, I think the following one is of interest, more especially since a definite "exciting cause" seems to have existed.

The patient, Mary M., aged 27, came to the Victoria Hospital for Diseases of the Nervous System, Belfast, on June 1, 1898, when the following history was obtained :—

Her parents and brothers and sisters are all healthy. She is a weaver by trade, and lived in the country until eleven years ago, and enjoyed good health up to about four years ago, when she had ten teeth extracted at one sitting without an anæsthetic. Immediately after this operation she commenced to feel unusually sleepy in the evenings, and soon afterwards began to sleep at her work, the sleep generally lasting from three to ten minutes at a time, and sometimes longer unless awakened. This sleep would overcome her under the most varied circumstances, and she found herself quite unable to prevent it. Between the attacks of sleep, which came on without warning, she felt quite clear, but complained of being more easily tired than natural. For some months after the extraction of the teeth she suffered from lightness in the head, with peculiar sensations passing over it from front to back, but these symptoms afterwards entirely disappeared.

On examination of the patient all the organs of the body were apparently healthy. She appeared mentally and physically lethargic, and walked slowly with a slight stoop. She had a heavy and rather sad expression, and her features were somewhat puffy. She slept from seven to eight hours per night.

The following notes were afterwards taken :—

March, 1899.—The patient has steadily improved, especially during the last six months, the sleeping attacks having decreased from about twelve or more a day to one, and sometimes there is perfect freedom from them for one, two, or even three days. She looks brighter, and the expression is more natural.

May.—The patient has not attended the hospital for some weeks, and the sleeping attacks have become much more frequent again. Since the last notes the patient has lost her father, and has had other worries.

June.—Much improved again.

Treatment.—The medicines which seemed to act best were phosphate of iron, sulphate of quinine, tincture of nux vomica, and nitro-glycerine. She has had galvanism applied three or four times a week, a current of one milliampere being allowed to flow through the head from before back for three minutes at a time. She was ordered nutritious and easily digestible dietary, moderate exercise, and as much fresh air as possible.

I think we have here a typical case of narcolepsy, as evidenced by the persistency to fall asleep twelve or fourteen times daily, the ease with which the patient was awakened, and the complete consciousness during the intervals.

No symptoms pointing to hysteria or epilepsy were present, and the attacks of sleep resembled in all respects "natural sleep"; the face remaining unaltered in colour, the sleep lasting for several minutes and often longer, and the patient being quite easily awakened into complete consciousness.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At the Clinical Meeting held on October 26, 1899, at 8.30 p.m., in the Medical Society's Rooms, 11, Chandos Street, the following cases were shown:—

Dr. J. A. Coutts and Dr. A. M. Gossage.—*Unusual cases of paralysis of acute onset occurring in brother and sister.*

(1) A girl, aged 5, while at Margate was suddenly attacked with general loss of power. On examination there was paralysis of all limbs and of the trunk, with general anæsthesia. No loss of power in face, tongue, diaphragm, muscles of deglutition, or in sphincters. Eye muscles also unaffected. Pain and tenderness in the course of peripheral nerves. Subsequent gradual recovery, except in the muscles of one shoulder.

(2) Her brother, aged 8, was attacked one week later after return to London. The general condition was exactly the same as that of his sister, except that there was no anæsthesia, and that the paralysis was less complete and did not last so long. Recovery was almost complete with the exception of the muscles of one shoulder.

Dr. James Taylor.—*A case of myopathy of the Landouzy-Dejerine type.*

The patient was a woman, aged 20 years. There was no history of myopathy among her relatives; an uncle and a cousin were insane. Since early infancy it had been noticed that she has been unable to completely close the eyes and that the face had a peculiar appearance. She had always suffered with epiphora and never been able to whistle. Weakness in the shoulder muscles came on two years ago and gradually increased.

P.S.—The appearance of the face was characteristic of the disease. Several of the facial muscles could not be demonstrated (platysma, risorius) and the others were very weak. There was some wasting of the tongue. The scapulæ were "winged." There were complete paralysis and great wasting of the latissimus dorsi, serratus magnus and of the trapezius on either side. The triceps was very weak and wasted on both sides. The other muscles of the body and limbs were well developed and powerful. The action of the levator anguli scapulæ and pectoralis minor in keeping the scapula against the thorax in the act of pushing forwards with the arm in the horizontal position was well shown.

Dr. Wilfred Harris.—*Case of myopathy of the Landouzy-Dejerine type.*

G. N., a stableman, aged 32, had noticed progressive weakness for the last six years. Mother, said to be similarly affected, died aged 65. None other of numerous family affected.

P.S.—Lordosis was marked, and the sternum much depressed. Rolling gait. Lips pouting, and paralysis of orbiculares oris et palpebrarum, and of zygomatici. Scapulæ elevated and winged, with paralysis and wasting of serrati magni, trapezius, latiss. dorsi, pectorals, right levator anguli scapulæ and right rhomboids, both biceps and triceps, supinator longus and extensors of fingers and wrists, with flexor contracture, and marked cyanosis of hands and forearms. There was weakness also of the abdominal muscles, glutei, hamstrings, and anterior tibial muscles. The electrical reactions were diminished, with sluggish contraction in wasted muscles to both currents, KCC > ACC. The left scapula hung higher than the right, owing to extra pull of lev. ang. scapulæ and rhomboid, while both scapulæ were much raised, and the superior angles everted by the pull of the anterior fibres of the deltoids and the supraspinati.

Dr. C. E. BEEVOR.—*A case of cerebral degeneration (diplegia).*

The patient was a boy, aged 14 years, whose family history was unimportant, and whose health up till the age of twelve years was excellent. At that time he had a severe febrile illness, which was said to be rheumatic fever. He recovered completely. Three months later he had another similar attack, and after two days' illness he became weak all over after having some sort of fit. After this his general health seemed to recover, but the limbs became gradually stiff and weak, and for three months his chin was turned to his right shoulder. He had some difficulty in swallowing at this time. During the last year the torticollis and stiffness in the arms had improved greatly, and he had developed intention tremor in the upper extremities. Mental state, intelligent. Speech slow. Deglutition slow. Nystagmus. Face rigid, and there is difficulty in the relaxation after effort. Slight rigidity and intention tremor of the upper extremities. Severe spastic paraplegia; trunk rigid. No sphincter trouble. Double foot clonus. Plantar reflexes showed an extensor response.

Dr. JAMES COLLIER for Dr. TOOTH.—*A case with acute onset resembling Friedreich's disease.*

The patient was a girl, aged 9 years. The family history was unimportant. At the age of eight years she had a febrile attack, and on the third day developed a convergent strabismus and great weakness of all the limbs, and she was unable to speak for a fortnight. She gradually recovered and regained her general health, but with returning power the limbs became extremely ataxic. They have improved slightly.

P.S.—There was marked mental dulness, convergent strabismus, extreme ataxy of all four limbs, lateral curvature of spine, very ataxic gait, deep reflexes absent. Plantar reflexes showed the flexor response. There was double pes cavus. Speech was slow, and the voice low pitched and monotonous.

BRAIN.

PART IV., 1899.

Original Articles and Clinical Cases.

SPINAL CORD CHANGES IN CASES OF CEREBRAL TUMOUR.

BY FREDERICK E. BATTEN, M.D.
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AND
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(1) Introduction and general statement of the changes found in the spinal cord in cases of cerebral tumour.
(2) Synopsis of previous observations on this subject.
(3) Suggested explanations of the changes found.
(4) Analysis of the cases.
    (*a*) Character of the degeneration.
    (*b*) Nature and situation of the tumour.
(5) Discussion of the cause of the spinal cord degeneration.
(6) The effect of operation; the condition of the knee-jerk and arm-jerks, and the presence of optic neuritis.
(7) Conclusions.
Appendix.
    Table of cases.
    Details of clinical history and pathological results.

I.

WHILE examining the spinal cords from cases that died of cerebral tumour, the fact that a considerable amount of degeneration was present in the posterior columns became apparent, and in order to determine what relation these changes bore to the symptoms present during life, and also to ascertain how frequently and to what extent these changes occurred, as many cases of cerebral tumour as could be obtained were examined, and, having lately had the opportunity of investigating some twenty-nine cases, we venture to bring the results under your notice. For the details of the clinical side of the cases, one of us (J. S. C.), and for the pathological investigation of the cases, the other (F. E. B.) is alone responsible, but for the views expressed we are jointly responsible. For permission to make use of these cases we would here acknowledge our indebtedness to Dr. Hughlings-Jackson, Dr. Buzzard, Dr. Bastian, Sir William Gowers, Dr. Ferrier, Dr. Ormerod, Dr. Beevor, Dr. Tooth, Dr. Taylor, Dr. Colman, and Dr. Risien Russell, of the National Hospital, and to Dr. Lees, of the Children's Hospital.

II.

Not a few authors have already written on this subject, and it will, therefore, be most convenient to give a short summary of their observations before we proceed to deal with our own cases.

Historical.

Degeneration of the posterior columns in cases of cerebral tumour has been noticed and recorded by several observers. C. Mayer, in 1894, in a paper, "Ueber anatomische Ruckenmarks befund in Fällen von Hirntumoren," was the first to recognise that the condition was associated with certain clinical phenomena, and to discuss its pathology.

In the above paper he refers to a paper published by Wollenberg, who described, in the case of a tumour of the left cerebellar hemisphere, a typical posterior degeneration extending from the lumbar to the cervical region, and affecting also the ascending roots of the fifth nerve and the posterior nerve-roots. The knee-jerks were absent, and the condition was regarded by Wollenberg as one of commencing tabes.

Two cases are described by Mayer, with loss of knee-jerk and early degeneration of the posterior columns.

Case 1 was that of a woman, aged 33, with aphasia and right hemiplegia, double optic neuritis, absent knee-jerks, but with active Achilles jerks. At the autopsy a tumour was found in the third left frontal region and operculum, and, on microscopical examination, degeneration was found in the posterior columns, but little marked in the sacral and lower lumbar region, more marked in the upper lumbar, dorsal, and cervical regions, and most marked in the column of Burdach in the last-named region. Lissauer's tract was unaffected, and no degeneration could be found in the extra-medullary portion of the posterior roots. Changes were noted in the cells of the anterior horns, but Clarke's column appeared quite normal.

In the second case, a man, aged 46, in whom symptoms had lasted for one year, and in whom the knee-jerks were absent, a tumour was found growing from the anterior extremity of the falx, and pressing on the frontal lobes. On examination of the cord, degeneration was found in the posterior columns, and especially in Burdach's column, and although some degeneration existed in the dorsal region, it was most marked at the level of the lower cervical roots. No degeneration could be found in the extra-medullary roots, and Clarke's column appeared to be normal.

That the condition is not one of early tabes is shown by the fact that the degeneration was more marked in the cervical than in the lumbar region of the cord, and affected the columns of Burdach to a greater extent than the column of Goll, and Lissauer's tract was unaffected.

That the condition cannot have been due to an affection of the spinal meninges was proved by the complete absence of any pathological change in these membranes.

In discussing the pathology, the author of this paper calls attention to the fact that in certain diseases the posterior columns are very liable to be affected, viz., ergotism, pernicious anæmia, lead poisoning, leprosy, alcoholism, Addison's disease, and like conditions; and he suggests that the degeneration above described may be due to some toxin in the altered cerebro-spinal fluid, which has been supposed to give rise to optic neuritis. Against such a theory the fact that the extra-medullary spinal roots, which are bathed with this fluid, escape, is brought forward. The question of the condition being due to increased intra-cranial pressure is then discussed, and, lastly, the condition of venous stasis produced by such an increase of pressure, the latter condition being thought the most probable origin of this degeneration.

In 1894, Campbell read before the British Medical Association, at Bristol, an account of two cases of softening of the cerebellum due to vascular change, associated with degeneration of the posterior columns.

In Case 1, a woman, aged 62, there had been paralysis of the left arm and leg for two years before death, and there was old softening and destruction of the greater part of the left cerebellar hemisphere, with degeneration in the left middle, inferior peduncles, the direct cerebellar tract, the ascending antero-lateral tract, and the posterior external columns of the left side; alteration in the nerve-cells in the region of the anterior cornu of the cervical region, and also degeneration in the left lateral pyramid. Clarke's column also appeared small.

In Case 2, a man, aged 73, with weakness of the left arm and leg, softening was present on the upper surface of the left cerebellar hemisphere, and degeneration was present in the left superior, middle, and inferior cerebellar peduncles; in the nucleus and funiculus cuneatus and in the posterior external columns of the cord. At the level of the sixth cervical root the degeneration occupied the outer half of Burdach's column. No degeneration could be traced below the level of the sixth dorsal root.

The author regards the degeneration of the direct cerebellar tract as a secondary atrophy, and not as a true degeneration; but the posterior degeneration he is inclined to regard as due to this part of the postero-external columns, being a direct descending cerebellar tract connecting the cerebellum with the lateral group of the anterior cornual cells of the lower cervical region of the same side. In a private communication; September, 1899, he states he is inclined to believe that this posterior degeneration is also a retrograde change, and not a true degeneration.

In 1895, Dinkler recorded a case of hydrocephalus and tumour of the right parietal lobe, with absent reflexes, associated with degeneration of the posterior columns, most marked in the cervical region and in the column of Burdach, and present also in the lumbar region of the cord. There was degeneration of the posterior roots. With regard to the pathology of this condition, after mentioning, he at once negatived, the possibility of the condition being due to involvement of the roots by growth secondary to that present in the brain, and suggested two other possible explanations:—(1) That the tumour produced some toxic substance; (2) that the condition was due to cachexia, since Oppenheimer and Siemerling have shown that degeneration of peripheral nerves may occur in cases dying of carcinoma, and the author inclined to this explanation of the condition.

In 1896, Pick described five cases :—

(1) A tumour in the posterior and median portion of the left cerebral hemisphere, with degeneration in the pyramid and in the posterior columns and in the posterior roots.

(2) A tumour in the left cerebral hemisphere, with degeneration most marked in the posterior columns in the lower cervical region, but also present in the lumbar cord.

(3) An osteo-sarcoma of the skull in a child, with degeneration most marked in Burdach's column, the posterior roots being unaffected.

(4) A glioma of both cerebral hemispheres, with no degeneration.

(5) A diffuse cerebral sclerosis, with degeneration of the posterior columns, most marked in the lower cervical region.

The author concluded that the condition was due to increased intra-cranial pressure, but why certain areas of the cord and roots were more affected than others he left for further observations to explain.

In 1896, Besold, in the case of two sisters, described degeneration of the posterior columns of the cord, most marked in Burdach's column and in the cervical region, associated with tumours in region of the third ventricle and optic thalamus. Degeneration was also present in

Gower's tract. The author attributed the condition to anæmia.

In 1897 Ursin described three cases :—

(1) A tumour in the left cerebral hemisphere with degeneration in the postero-external columns, leaving the septo-marginal, the cornu-commissural zone, and Lissauer's tract unaffected. The extra-medullary portion of the posterior roots were affected, and some alteration in the cells of Clarke's column was present in the dorsal region. The degeneration was most marked in Burdach's column, and was not present above the posterior column nuclei.

(2) Two tumours, one in the left occipital lobe and another in the right frontal lobe. The cord showed degeneration in the posterior columns most marked in Burdach's column. The posterior roots, Lissauer's tract, and Clarke's column showed no change. There was degeneration in the lateral columns.

(3) A tumour in the left optic thalamus, with degeneration in both pyramidal tracts, diffuse degeneration in the posterior columns, and also in the intra-medullary portion of the hypoglossal nerve of the right side. No degeneration was present in the extra-medullary roots or in Lissauer's tract.

He considered that the condition was not due to increased intra-cranial pressure, but to an intoxication and a failure of nutrition.

In 1897 Hoche described three cases :—

(1) A tumour in the right cerebral hemisphere with degeneration in the left pyramid and in the posterior columns. The extra-medullary roots were unaffected, and the change was more marked in the cervical than in the dorsal or lumbar region.

(2) A tumour in the left lateral lobe of the cerebellum, with degeneration in the posterior columns, more marked in the cervical and lumbar regions than in the dorsal. The extra-spinal roots were unaffected.

(3) A tumour growing from the dura mater, and pressing on the left cerebral hemisphere. The spinal cord showed no degeneration.

The author concluded that neither the age of the patient nor the situation, nor the histological characters of the growth, were in causal relationship with the degeneration of the posterior columns, but that the condition was dependent upon increase of intra-cranial pressure.

In two of the cases above reported there was optic neuritis and degeneration of the posterior roots, while in the third there was no optic neuritis and no degeneration of the posterior roots.

In 1899 Bikeles described posterior degeneration occurring in a patient who died twenty days after being shot in the right frontal region. The injury gave rise to left hemiplegia. There was degeneration in the right pyramid and in the column of Goll from the mid-dorsal to the cervical region. This degeneration was most marked on the side of the affected pyramid. There was also degeneration of the first cervical root on the right side.

The suggested explanation of the condition was that the disturbance caused by the bullet wound was conveyed to the spinal cord through the cerebro-spinal fluid and affected the most vulnerable portions, viz., the posterior columns, although the effect of toxin could not be excluded since suppuration and encephalitis were present in the region of the injury. With regard to the first cervical root which showed degeneration, not only in its intra-spinal course, but also in its extra-spinal course, it was suggested that the sudden movement of the cerebro-spinal fluid owing to the entrance of the shot would be especially liable to injure this root on account of its close proximity to the foramen magnum.

Digest.

In the above papers there are fifteen cases of cerebral tumour showing degeneration in the posterior columns and two cases with negative results so far as the cord is concerned. In addition to these there are two cases published by Campbell with degeneration in the posterior columns in which there was no tumour, but thrombosis of some cerebellar vessel. In twelve of the above cases, at any rate, the degeneration was most marked in the lower cervical region, and in only four of these was there degeneration in the extraspinal posterior roots.

III.

It will be gathered from the above digest that various suggestions have been brought forward to account for this posterior degeneration, and of these the following may be at once rejected:—

(1) That the condition is one of early tabes.

(2) That the condition is due to involvment of the posterior roots by secondary deposits from growth in the cranium.

(3) That the condition is secondary to some spinal meningitis or thickening of the membranes.

(4) That the condition is due to a descending degeneration in the posterior columns. (Under this heading retrograde degeneration is not included, as this will be discussed later on.)

Passing now to the consideration of the various conditions which may reasonably account for this spinal change, one may discuss them under the following heads:—

(1) A toxic agent. (*a*) Produced by the tumour itself. (*b*) Secondary to the anæmia and cachexia resulting from the tumour.

(2) Increased pressure in the cerebro-spinal canal.

(3) Venous stasis, anæmia, thrombosis in the spinal vessels secondary to the increased pressure.

(4) Retrograde degeneration.

(1) (*a*) *A toxic agent produced by the tumour.*—Assuming that it is possible for a malignant growth to produce a toxin either by its own activity or by the destructive change in the cerebral substance in which it grows,[1] is it possible that such a poison would exert a selective action on certain portions of the nervous system? (for instance, the posterior

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[1] MOTT AND HALLIBURTON, *Philosophical Transactions*, vol. cxci., p. 211-267. Mott and Halliburton have shown that the body "choline," formed from the destruction of lecithin, is present in the cerebro-spinal fluid of patient suffering from general paralysis of the insane, and that injected into animal it produces certain toxic effects.

nerve roots). In reply to such a question the state of things met with in tabes, pellagra, and ergotism, besides other conditions, might be cited as instances where a poison exerts such a selective action. On the other hand, the selective action in the present case seems almost more limited than in the conditions above named, for almost all observers are agreed that the degeneration affects the lower cervical region to a greater extent than any other portion of the cord, and the same is borne out in the present series of cases, though it is by no means invariable, for in two cases (Nos. 19 and 27) the degeneration was as marked in the lumbar region of the cord as in the cervical.

That posterior degeneration is more marked in cases where the tumour is of rapid growth and invades the cerebral substance is certainly born out by the present series of cases, but there are other conditions accompanying such rapid growth which may exert a harmful influence on the posterior roots, and the effect can hardly be attributed to the action of a toxin.

(*b*) *A toxic agent secondary to the anæmia and cachexia produced by the growth.*—It is hardly possible to maintain such a view, for *it is well known that* patients suffering with cerebral tumours rarely emaciate to any marked extent, and are often well nourished. In 140 consecutive cases of intracranial tumour examined by one of us (J. S. C.) at the National Hospital, general wasting was observed in seven cases only, and in each case a complication was present to account for such wasting, *i.e.*, tubercular meningitis, once; tubercular peritonitis, once; carcinoma of lung, once; prolonged stupor with the attendant difficulties of administering nourishment, four times.

The marked hemiplegic and general wasting, not infrequently observed after the removal of intra-cranial growths by operative measures, is not considered among these cases.

In six cases where the symptoms were of long duration (upwards of eighteen months), and where the growth was of large size and situated in the cerebral hemispheres, the patients were very well nourished at the time of death.

In the series of cases here recorded wasting was a marked feature in four cases only, Nos. 5, 12, 18, and 21, and these cases were well nourished until operative measures for the removal of the growth had been resorted to. In the cases, Nos. 18 and 21, where emaciation was extreme, no degeneration of the posterior columns was present.

It should, however, be borne in mind that Oppenheimer and Siemerling have shown that changes are sometimes found in the peripheral nerves in cases of carcinoma. That the condition cannot depend on simple marasmus is shown by the fact that in three cases of extreme wasting due to tubercle examined by Mayer no change could be found, nor can it be due to anæmia alone, for I have examined cords in extreme anæmic conditions with a negative result.

(2) *That the condition is due to increased pressure in the cerebro-spinal canal* is a view that would seem to be the most reasonable explanation, and even if it is not the sole cause of the condition, it is most certainly an important factor in the ætiology of the condition. There are, however, various arguments against such a view.

Firstly, it is urged that if the condition is due to increased pressure, then the degeneration should be most marked in the lumbar region where the fluid pressure is greatest. On the other hand, the point at which the degeneration is most marked is the cervical region, an objection, however, that does not carry much weight in that many patients who present these changes in the cord are unable to maintain the erect position, and, therefore, in them the pressure is not greater in the lumbar than in the cervical region.

Secondly, there are cases in which there is no increase in the intra-cranial pressure, and yet degeneration of the posterior columns has been present. Moreover, the cases reported by Dr. Campbell, of Rainhill, might be cited in this connection.

Thirdly, the degeneration is stated to be often asymmetrical, whereas if it had been due to pressure one would have expected it to have been symmetrical. In this relation, however, it must be pointed out that the asymmetry of the lesion is very slight as a rule, so that little can be based on this point.

Fourthly, the degeneration is often limited to the cord and the posterior roots are unaffected, whereas the roots are more exposed to pressure than is the cord.

Such are the arguments against the pressure theory, but there is no doubt that the degeneration is present in its most marked extent in those cases in which the rise of intracranial pressure has been rapid. In the chronic cases where there is marked hydrocephalus the degeneration is often slight or absent.

(3) *Venous stasis, anæmia, or thrombosis in the spinal vessels secondary to the increased pressure.*—Direct evidence on this point is wanting, for in all the cases examined there is no evidence of thrombosis of the smaller vessels; sometimes they are full and engorged, at other times empty. However, the change in the cord is never a localised patch of softening or myelitis such as one might expect to find if there were actual thrombosis of some of the smaller vessels, nor is there anything to suggest that the change is due to hæmorrhage. There is no evidence pointing to the posterior root ganglia being the seat of the lesion; indeed, such evidence as there is is directly opposed to this, for in those cases in which the ganglia have been examined they have been found to be normal. The posterior roots are often unaffected, and even when affected the degeneration is always less than in the posterior columns of the cord. The affection of the direct cerebellar tract is uncommon, and does not necessarily occur in cases of cerebellar tumour. In one case (No. 1) in which it was most marked it was symmetrical, and only extended down to a point between the first and second cervical. There were a few degenerate fibres below this level, but they could not account for the marked degeneration above this level. There was no evidence of myelitis in this region, but that there must have been some pressure at this level, viz., first and second cervical, is borne out by these two facts, viz., that there was marked degeneration in the direct cerebellar tracts above that level, and there was an increase in the degeneration in the pyramidal tracts below that level. Such a condition is not common, and occurred in only two other cases (Nos. 5 and 20), and in the

former of these the degeneration in the posterior columns only became marked above the level of the second cervical.

(4) *Retrograde degeneration.*—This view was advanced by Dr. Campbell in his most interesting report of cases of softening of the cerebellum, with degeneration in the posterior columns and the direct cerebellar tract, but although his arguments are applicable in the cases he brings forward, yet such an explanation cannot account for the condition met with in the present series of cases, except so far as the extra-spinal posterior roots are concerned. This point will be further discussed in the latter portion of this paper.

IV.

Twenty-nine cases have been examined, and the accompanying table indicates their situation and the amount of degeneration that occurred in the posterior columns. For the sake of classification the degeneration has been placed under the three heads, "Marked," "Slight," and "None."

TABLE I.

	No. of cases.	No degeneration.	Slight degeneration.	Marked degeneration
Frontal	6	2	2	2
Parietal	2	1	1	0
Temporo-sphenoidal ..	7	1	2	4
Cerebellar	9	3	2	4
Basal ganglia and pons ..	5	2	2	1
	29	9	9	11

From the analysis shown in Table I. it would appear that degeneration is rather more liable to occur with tumours in the temporo-sphenoidal region than when situated elsewhere, and also that a tumour situated behind the parietal region is more liable to give rise to degeneration than one more anteriorly situated.

(*a*) *Character of Degeneration.*

The degeneration is of such a character that though readily shown by the Marchi method, is not well-marked by the Weigert-Pal method. The degeneration affects the posterior columns of the cord, and in all cases, except No. 27, is more marked in the cervical than in other regions. It therefore follows that the postero-external column (Burdach) is more affected than the postero-internal (Goll). The degeneration is of root origin, for in many cases it can be seen limited to a region occupied by the ascending fibres of a root, and the endogenous tracts tend to escape. It cannot be said, however, that these tracts contain no degenerate fibres, but fewer than the tracts of exogenous origin; and although the endogenous tracts are, for the most part, composed of fibres derived from within the cord, yet few will deny that they contain also fibres of exogenous origin.

In one case, No. 6, the degeneration was limited to one root, viz., the fifth lumbar, and this degeneration was so marked that it might be considered fortuitous; and in another case, No. 15, it was limited to two roots, the sixth and seventh cervical. In the cases 10, 11, 19, 27, degeneration was well marked in the whole of the posterior columns of the cord, from the cervical to the lumbar region, but in the remaining cases the condition, although not limited to the cervical region, showed comparatively little or no degeneration in the dorsal and lumbar region.

The degeneration could be traced up to the posterior column nuclei, and as the column of Burdach was most affected in the cervical region, so the degeneration was more marked in the funiculus cuneatus than in the funiculus gracilis.

Lissauer's tract.—A few degenerate fibres were present in this tract in two cases, Nos. 10 and 11, but in neither was this marked, and in the remaining cases the tract appeared perfectly normal.

The fillet.—Slight degeneration was present in five cases, Nos. 5, 11, 12, 26, and 27, but in none was it marked nor in any way proportional to the amount of degeneration in the posterior columns.

The direct cerebellar tract.—There was degeneration in this tract in three cases; in all three it was symmetrical, and in case No. 1 it was only present above the level of the second cervical root; in cases Nos. 12 and 20, as no examination of the cord was allowed, it was impossible to say from what point it extended. It has been shown by Dr. Leonard Hill ("Allbutt's System of Medicine," vol. vii.), that when the intra-cranial pressure is rapidly increased, the cerebellum and the bulb descend and completely block the foramen magnum, and, from the altered position of the parts, pressure must be brought to bear on the upper region of the cervical cord, and this gives a ready explanation for the degeneration in the direct cerebellar tract.

Posterior roots.—Degeneration of the posterior roots was present in five cases, and in one other to a slight extent; it was always considerably less than the degeneration in the posterior columns.

Posterior root ganglia.—In a few cases these have been examined, but with negative results.

Cranial nerves.—In case No. 1 the intra-medullary portion of the twelfth nerve on one side was found to be degenerate; the cause of this degeneration could not be found, but as there was a localised patch of softening in the upper portion of the pons, a similar patch may have occurred near the twelfth nucleus, and thus have given rise to this degeneration.

In case No. 12 there was degeneration of the seventh nerve on one side; the origin of this also was not found.

(*b*) *Nature of Growth.*

The growth varied greatly, not only in external but also in microscopical appearances, and the following table gives the number in each group:—

TABLE II.

Nature of growths.

Tuberculous	2
Gummatous	1
Glioma	5
Psammoma	1
Cyst of choroid plexus	1
Sarcoma (under this head are included fibro-alveolar, glio-, and irregular-celled sarcomata as well as endothelioma)	18
Not examined	1

V.

The cause of the spinal cord degeneration may be conveniently discussed under the following heads.

(1) Does the condition depend on the situation of the tumour?

(2) Does the condition depend on the nature of the tumour?

(3) Does the condition depend on the increase of intracranial pressure and the rapidity with which such increase occurs, or is it a combined effect of the increased intracranial pressure with dilatation of the ventricles, or is it dependent on the latter factor alone?

(1) *Does the condition depend on the situation of the tumour?*

In answer to this question, if one takes the cases in which the posterior degeneration is most marked, viz., 1, 10, 11, 12, 19, 27, one finds that the first is a frontal tumour, the next three are temporo-sphenoidal, the fifth a cerebellar tumour, and the sixth a tumour of the corpora quadrigemina; that is to say, degeneration may occur in whatever portion of the brain the tumour is situated, but that growths in the temporo-sphenoidal region are more frequently accompanied by marked degeneration than tumours in other situations, and the same is borne out if one takes all the cases in which posterior degeneration occurs, as shown in the following table:—

TABLE III.

Frontal	4
Parietal	1
Temporo-sphenoidal	6
Cerebellar	5
Basal ganglia	3

It is, however, obvious from consideration of the above figures that the situation of the tumour alone can have little influence on the occurrence of this posterior degeneration.

(2) *Does the condition depend on the nature of the tumour?*

In considering this question, if one again takes the cases in which degeneration is most marked, viz., 1, 10, 11, 12, 19, 27, one finds No. 1 is a glio-sarcoma, No. 10 is a glioma, No. 11 is a spindle and round-celled sarcoma, No. 12 is an irregular-celled sarcoma, No. 19 is a glioma, No. 27 is a round-celled sarcoma; that is to say, all are comparatively rapidly-growing tumours. On the other hand, if one takes the cases with no degeneration, one finds No. 2 is a sarcoma, No. 3 is a gumma, No. 7 nature uncertain, No. 14 is a spindle-celled sarcoma, No. 16 is a glioma, No. 18 is a tuberculous growth, No. 21 is a fibro-sarcoma, No. 28 is a glioma, No. 29 is a cyst of the choroid plexus; that is to say, a mixed variety of tumours, the majority of which were of chronic nature, but three, at any rate, were of rapid growth. Therefore, it would seem that though the nature of the tumour may be a factor owing to its rapid increase in size, it cannot be considered to play any part with regard to the production of posterior degeneration so far as any toxin which it is supposed to form is concerned.

(3) *Does the condition depend on the increase of intra-cranial pressure and the rapidity with which such increase occurs, or is it a combined effect of the increased intra-cranial pressure with dilatation of the ventricles, or is it dependent on the latter factor alone?*

Nearly all the cases showed increase of intra-cranial pressure either at the time of death or previous to operation. In two cases of long standing (16 and 21) there was no evidence of increased intra-cranial pressure, the lateral ventricles being, however, in both cases very considerably dilated but the cord in these cases showed no change. This would seem to suggest that dilatation of the ventricles alone does not give rise to posterior degeneration.

Taking then the case in which the posterior degeneration was most marked, viz., No. 27, it was found that a large rapidly-growing tumour (nine weeks) existed in the optic thalamus and corpora quadrigemina, causing obstruction to the Sylvian aqueduct and marked dilatation of the ventricles. The degeneration extended the whole length of the spinal cord and affected both the columns of Burdach and Goll. Such a case would seem to point to the condition being due to the rapid increase in intra-cranial pressure, together with dilatation of the ventricles. This is not, however borne out on examination of the other cases in which the degeneration is most marked, for in the cases 11 and 19 there was no distention of the ventricles. Increased intra-cranial pressure was, however, present, and in one of the cases was limited to the subtentorial region. The one common factor in nearly all the cases seems to be increased intra-cranial pressure, but even when this is present and has been of rapid onset, cases occurred (Nos. 2, 14, 28, 29) in which no spinal degeneration was present. These exceptions, however, admit of an explanation. No. 2 was a frontal tumour, and posterior degeneration seems to occur less frequently with tumours in this situation, and in Nos. 28 and 29 the pressure symptoms had existed a comparatively short time.

The evidence, as gathered from the above series of cases, seems to point to the rapid increase of intra-cranial pressure, especially when associated with dilatation of the ventricles as the cause of the condition. The question then arises: How does such intra-cranial pressure account for degeneration in the posterior columns of the cord? In an article by Dr. Leonard Hill on the experimental pathology of cerebral circulation, he shows that the intra-cranial pressure does not exceed the normal cerebral venous pressure, and makes the following statement:—" Since at any pressure above cerebral venous pressure the cerebro-spinal fluid rapidly leaks away from the cranial cavity, this fluid can be entirely neglected in dealing with the pathology of compression. It is absolutely erroneous to teach that increased cerebral pressure is transmitted to all parts of the cranio-vertebral cavity by the cerebro-spinal fluid. It is equally erroneous to teach that a foreign body within the cranium exerts pressure."

Such a statement as the above makes it extremely difficult to account for posterior degeneration on the increased pressure theory. On the other hand, when one sees the distended ventricles, the dilated posterior cistern and the distended arachnoid space in the spinal cord, one cannot but think that the increased fluid pressure within the ventricles is communicated to the spinal canal. In order to obtain further evidence on this point the spinal canal and the theca were carefully opened so as not to injure the arachnoid; fluid was injected into the ventricles under a pressure of a column of water 2 ft. high, and as the arachnoid became distended it was seen that the spinal roots which, under normal conditions, lie close to the cord and pass in a nearly straight line from their point of exit on the dorsal side of the cord to their point of passage through the theca, were carried away from the cord owing to their attachment to the arachnoid, and formed a bow instead of a straight line, the curve being most acute where the roots passed into the spinal cord. The anterior roots being less attached to the arachnoid membrane than the posterior would be less liable to suffer when the sub-arachnoid space is distended. If the pressure between the dura mater and the arachnoid be the same as that in the sub-arachnoid space, then no stretching of the roots will take place; and this fact may account for the absence of degeneration in certain cases of marked intra-cranial pressure. It is therefore probable that the point at which the root is most likely to suffer is that at which it enters the spinal cord. And it has been shown that at this point it becomes constricted, and the medullation of the fibres becomes thinner and often seems almost to disappear altogether leaving the naked axis-cylinder; traction, therefore, either in the normal direction of the root, or still more in some altered direction, would be extremely liable to injure it at this point.

Now, the fact that the posterior columns of the cord are often affected without the roots showing any or very slight change, is proved in cases Nos. 11, 13, 27, in which the cord is affected, and little or no change could be found in the roots; and in other cases where degeneration is present in the roots it is slight in comparison to the amount of change in the posterior columns of the spinal cord. The explanation of such a condition is clear, namely, that degeneration occurs in the portion of the neuron distal to the injury, *i.e.*, that in the posterior columns, while only a slow "retrograde" degeneration occurs in the root proximal to its connection with the ganglion. That such an explanation can account for the fact that the lower cervical roots are more liable to be affected than the dorsal and lumbar is probable, owing to their shorter course, and, therefore, greater traction.

VI.

Operation can have no direct effect in causing posterior degeneration; twelve cases were operated on, and in eight degeneration was present, and in four there was no degeneration

Age.—The ages of the patients varied from 1½ years to 64 years. Eight were under the age of 10; in six of these eight cases the tumour was situated in the cerebellum, in the seventh in the pons, and in the eighth in the corpora quadrigemina and optic thalamus. Of these eight children, in five posterior degeneration was present, while in the remaining three no degeneration could be found. It is, therefore, certain that age has no influence on the occurrence of this degeneration.

The knee-jerk.—The knee-jerks were absent in seven cases (9, 10, 14, 19, 24, 25, 27), and were diminished or absent on one side in five other cases (11, 13, 15, 22, 23).

Now, all these cases, except No. 14, showed some degeneration, and it was marked, not only in the cervical region, but also in the lumbar, in all the members of the first group, except Nos. 24 and 25.

It will be noted that of the cases with absent knee-jerks, Nos. 9, 10, 14 are tumours of the temporo-sphenoidal lobe, and that Nos. 25 and 27 are tumours of the choroid plexus and corpora quadrigemina respectively, and that Nos. 19 and 24 were cerebellar tumours.

That the presence or the absence of the knee-jerks is connected with the presence or absence of posterior degeneration in the lumbar region of the cord is, certainly proved in many of the cases here recorded, but such an explanation will not suffice, however, in every case.

The presence of the knee-jerk does not negative the possibility of posterior degeneration, for other conditions may tend to bring about the preservation of the jerk, notwithstanding the presence of posterior degeneration in the lumbar region, *e.g.*, the occurrence of degeneration in the pyramid.

The absence of the knee-jerk in cases of cerebral tumour, when the observation is made before the supervention of coma or the last stages of the disease would seem to indicate degeneration of the posterior columns.—Case No. 14 might be cited as a case to the contrary, but it was only towards the end that the knee-jerks were abolished, and accurate observations were not made until the patient was already in a drowsy condition. Case No. 15, in the second group of cases in which the knee-jerks were diminished, is more difficult of explanation, for although degeneration was present, it was only present in the cervical region.

Special attention has been drawn to the absence of the knee-jerk in tumours of the temporo-sphenoidal lobe by Coxwell, Stephen Mackenzie, and Hughlings Jackson. In 160 cases of intra-cranial tumour where the position of the tumour was ascertained *post mortem*, occurring at the National Hospital from 1883-1897, the knee-jerks were absent in 10 per cent. of the cases, and in twelve of these sixteen cases the tumour was situated in the cerebral hemispheres, and in three in the cerebellum.

In order to determine whether the condition of posterior degeneration was evidenced clinically by a loss of the supinator and triceps-jerks, the deep reflexes were examined—(*a*) in 100 healthy persons in whom they were readily elicited without any exception ; (*b*) in 120 consecutive cases of intra-cranial tumour under the care of one of us (J. S. C.) during the last three years at the National Hospital in which these phenomena had been carefully recorded, the arm-jerks were absent in twenty-five cases = 20 per cent., whereas the knee-jerks were absent in twelve cases = 10 per cent. Both arm and knee-jerks were absent on one side in two cases, and the arm-jerks were absent on one side in one case. In four cases the arm and knee-jerks were variable, sometimes present, sometimes absent, and in these cases the cerebellum was the seat of disease. From this it would appear that consequent upon the greater frequency of the incidence of the posterior degeneration upon the cervical region, the absence of the arm-jerks in cases of intra-cranial tumours is twice as common as is the absence of the knee-jerk, and that variable deep reflexes, now present, now absent, are met with in connection with subtentorial growths.

We do not advance posterior degeneration as the cause of the loss of deep reflexes in all cases of intra-cranial tumour where such loss occurs. We have noticed sudden and persistent loss of these signs in several cases of vascular cerebral disease and in cases of cerebral tumours, and for these cases there must be some other explanation.

In connection with the symptomatology arising from the posterior degeneration, we have seen several cases of intra-cranial tumour in which marked hypotonia, severe lightning pains, and ataxy of tabetic type were present.

Optic neuritis.—This, in its early, marked, or late form of atrophy, was present in all cases except one (No. 27), and in this case there was marked degeneration of the posterior columns of the spinal cord.

Neuritis was present in nine cases in which there was no posterior degeneration, and in nineteen in which posterior degeneration occurred. And although it is possible that the two conditions may have a common cause, it cannot be assumed that when neuritis is present posterior degeneration is likewise present, nor when the former is absent the latter is likewise absent.

VII.

CONCLUSIONS.

(1) That degeneration of the posterior columns of the spinal cord frequently occurs in cases of intra-cranial tumour, *i.e.*, about 65 per cent.

(2) That such degeneration is more liable to affect the spinal cord in the cervical region than in the dorsal or lumbar regions, and is more marked in the postero-external than in the postero-internal columns.

(3) That such degeneration is of root origin, and arises from the point where the root enters the spinal cord; the posterior roots are always less affected than the posterior columns, and may show no degeneration.

(4) That such degeneration is due to traction on the posterior roots by the distension of the arachnoid, owing to the increased intra-cranial pressure, and especially such as tends to rapid dilatation of the ventricles and the sub-arachnoid space in the spinal cord.

(5) That such degeneration is independent both of the situation and of the nature of the tumour, except in so far as their liability to give rise to the preceding condition is concerned.

(6) That optic neuritis bears no relation to the occurrence of posterior degeneration.

(7) That absence of the knee-jerks (except in the semi-comatose state) indicates posterior degeneration, but that their presence does not negative such a condition, and absence of the arm-jerks has the same significance.

(8) That degeneration may occur in the direct cerebellar tract; such degeneration being directly due to pressure on the cervical region of the cord.

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GENERAL EXPLANATION OF FIGURES AND DIAGRAMS.

The reproductions of the tumours in the brain are from photographs taken after the brain had been hardened in formalin solution.

The diagrams of the cord are from sections stained by the Marchi method, and have been drawn under an Edinger's projection apparatus.

The areas of degeneration have been indicated whilst the slide was in position, whenever this has been possible; but owing to the low magnifying power of the apparatus, it is often impossible to indicate the slighter amounts of degeneration, and these have been filled in subsequently under the microscope.

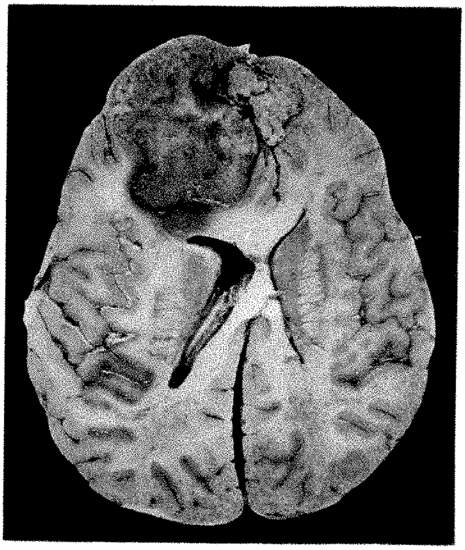
It is impossible to represent every degenerate fibre by a dot, which is relatively too large, but an endeavour has been made to keep the relative amount of degeneration in the various sections as accurate as possible.

CASE 1.

Tumour of the left frontal lobe. (Glio-sarcoma.)

Sections of the medulla and spinal cord show:—(1) Degeneration in the postero-external column in the cervical region ascending to the posterior column nuclei; (2) Degeneration in the direct cerebellar tracts above the level of the 2nd cervical; (3) Degeneration of the pyramids, most marked below the level of the 2nd cervical but present also above; (4) Degeneration in the intra-medullary portion of the 12th nerve.

PLATE I.



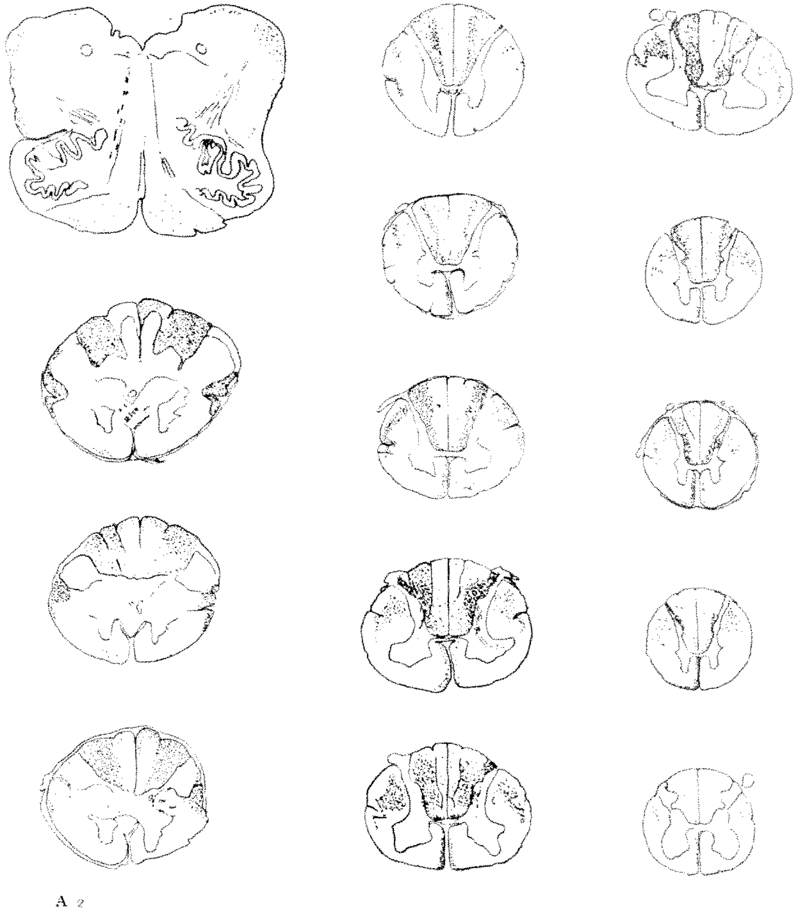
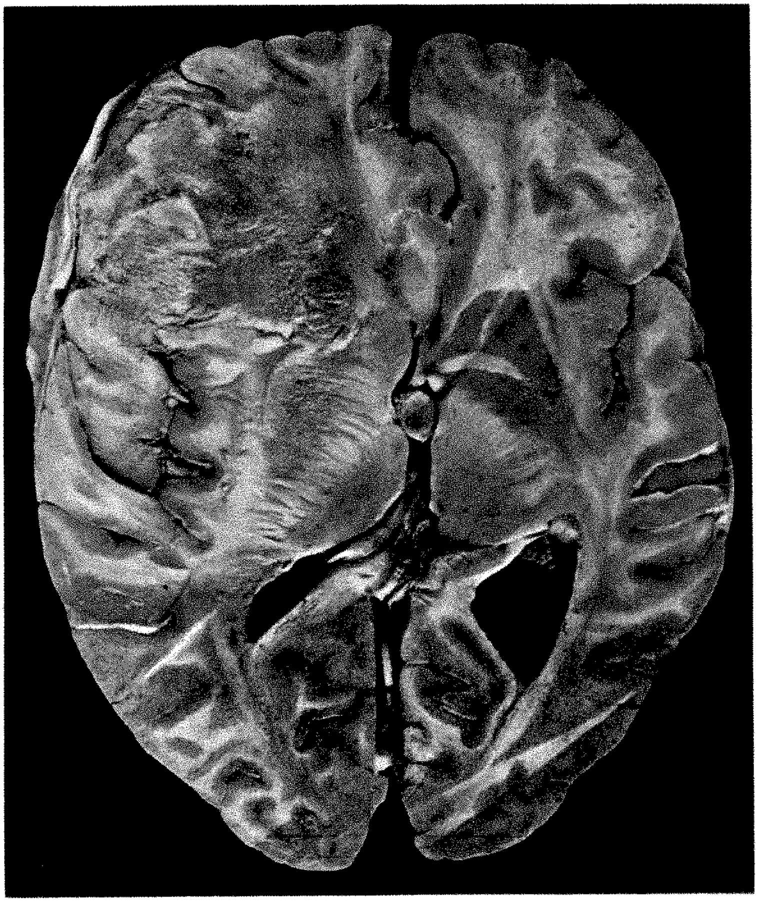


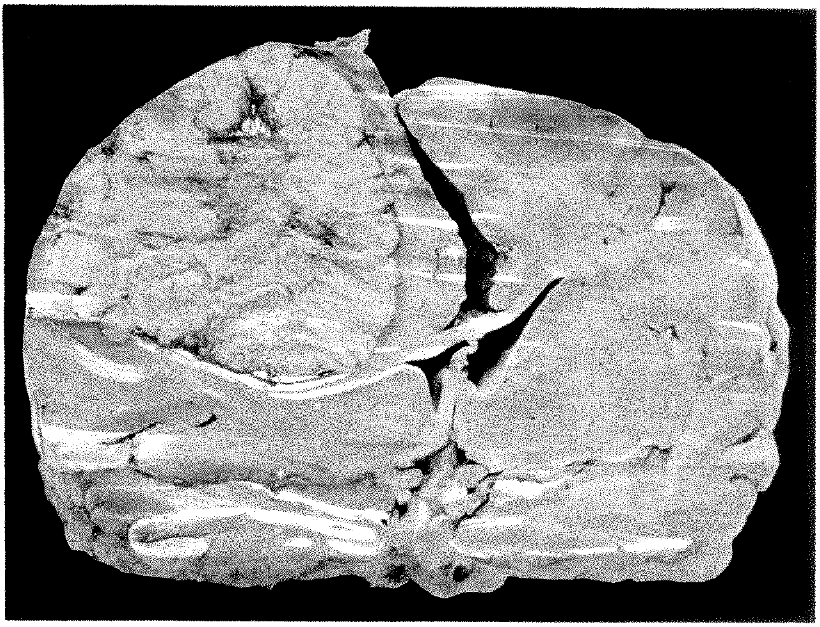
PLATE II.

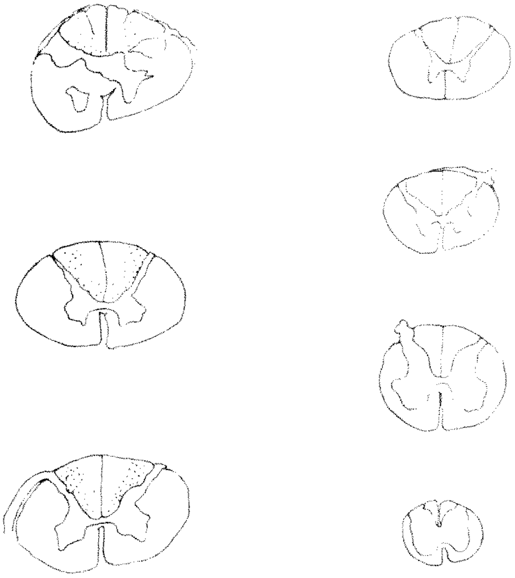


Case 2.

Tumour of the left frontal lobe. (Mixed-celled sarcoma.)
The cord shows no degeneration.

PLATE III.





CASE 4.

Tumour of the right frontal lobe. (Psammoma.)

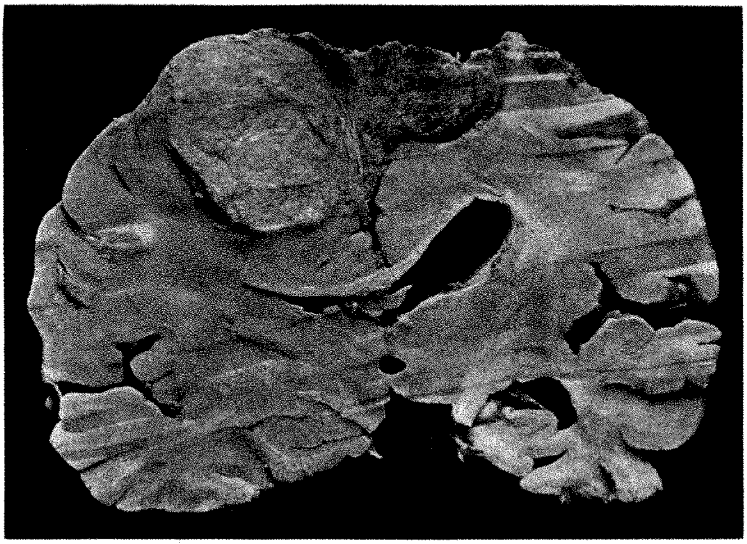
The cord shows slight degeneration in the posterior columns in the cervical region, and a few degenerate fibres are also present in the dorsal and lumbar region.

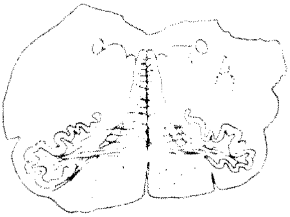
CASE 5.

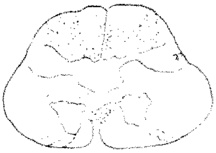
Tumour of the right and left frontal and parietal regions. The tumour was removed from the right side. (Alveolar sarcoma or endothelioma.)

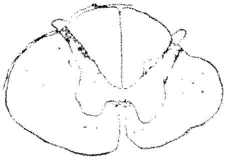
The cord shows degeneration in the posterior columns above the level of the 1st cervical but none below this point, although there is some degeneration in the crossed pyramidal tracts.

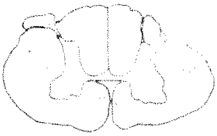
PLATE IV.

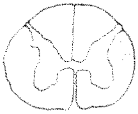


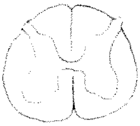


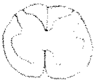


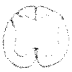












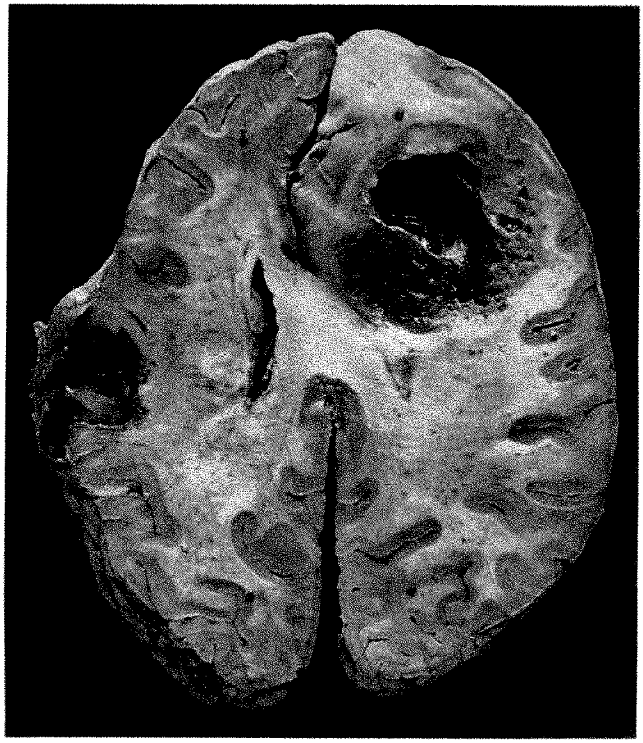
CASE 6

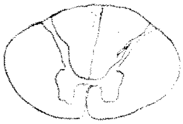
Tumour of the right frontal lobe. (Glioma.)

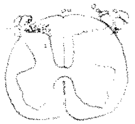
The degeneration in the cord is limited to the 5th left lumbar root, and this can be traced up through the dorsal to the cervical region.

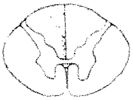
There is also degeneration in the posterior root from its exit from the posterior root ganglion to its entrance into the cord. The degeneration is more marked by the Weigert-Pal method than by the Marchi method, and is evidently of long standing. It is, probably, therefore a fortuitous condition, and unconnected with the presence of the cerebral tumour.

PLATE V.









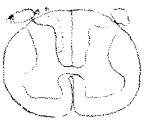
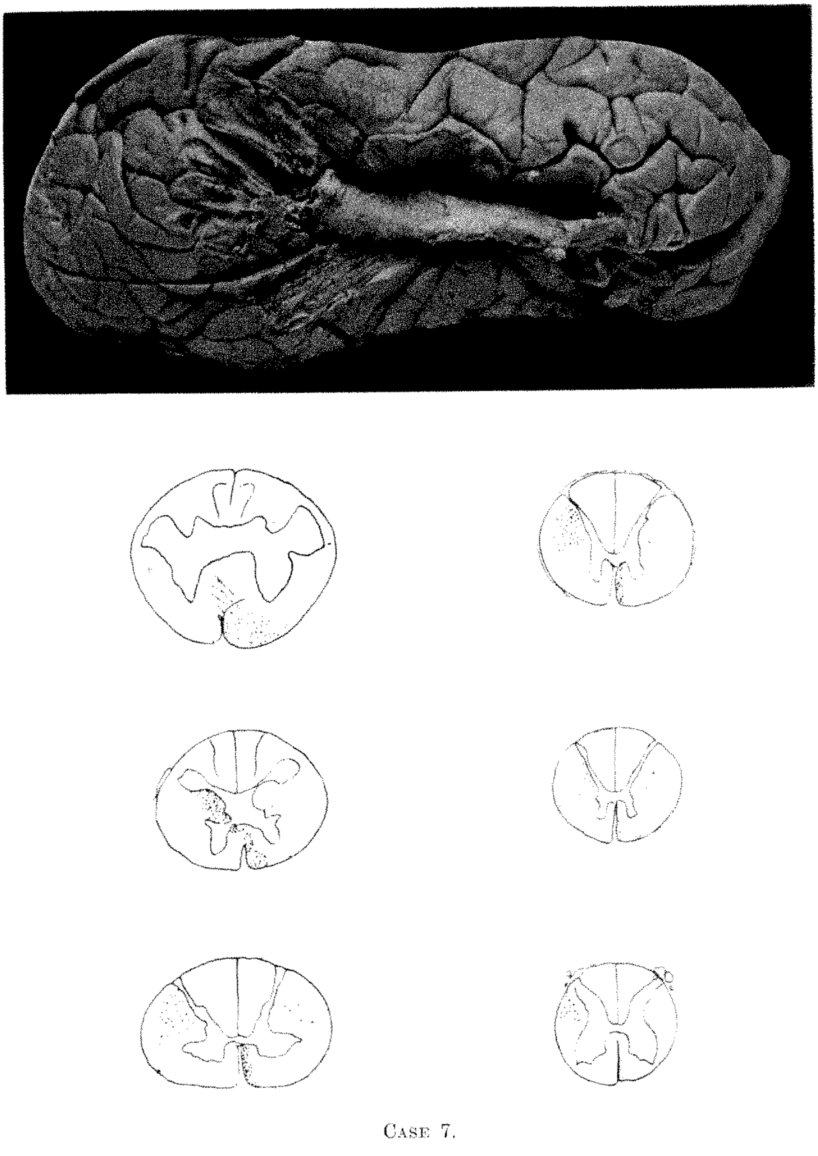


PLATE VI.



Case 7.

Tumour of the right motor region (removed by operation).

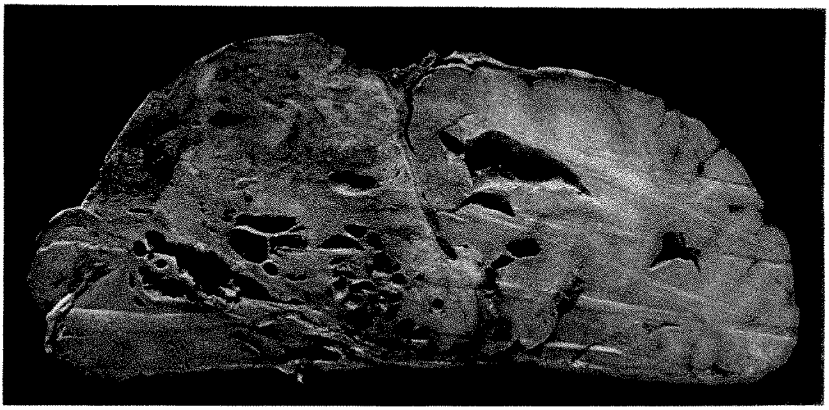
The cord shows no lesion of the posterior columns, but marked degeneration in the left crossed and right direct pyramidal tracts.

CASE 8.

Tumour of the right hemisphere partly removed by operation. (Mixed-celled sarcoma.) The multiple cystic condition present in the neighbourhood of the tumour is due to *post-mortem* emphysema which has occurred in this region.

The cord shows slight degeneration of the posterior columns, and marked degeneration of the left crossed and right direct pyramidal tracts and some degeneration of the opposite tracts.

PLATE VII.



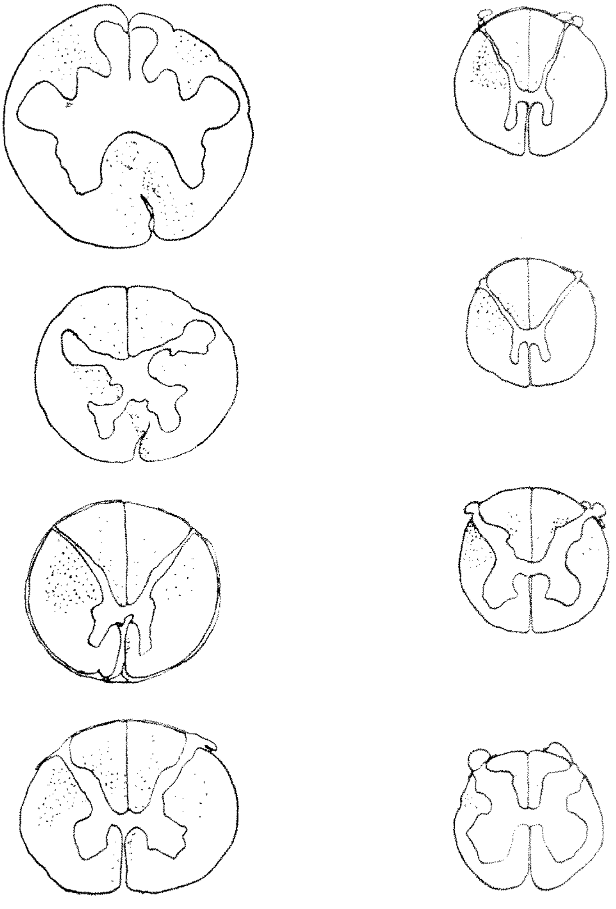
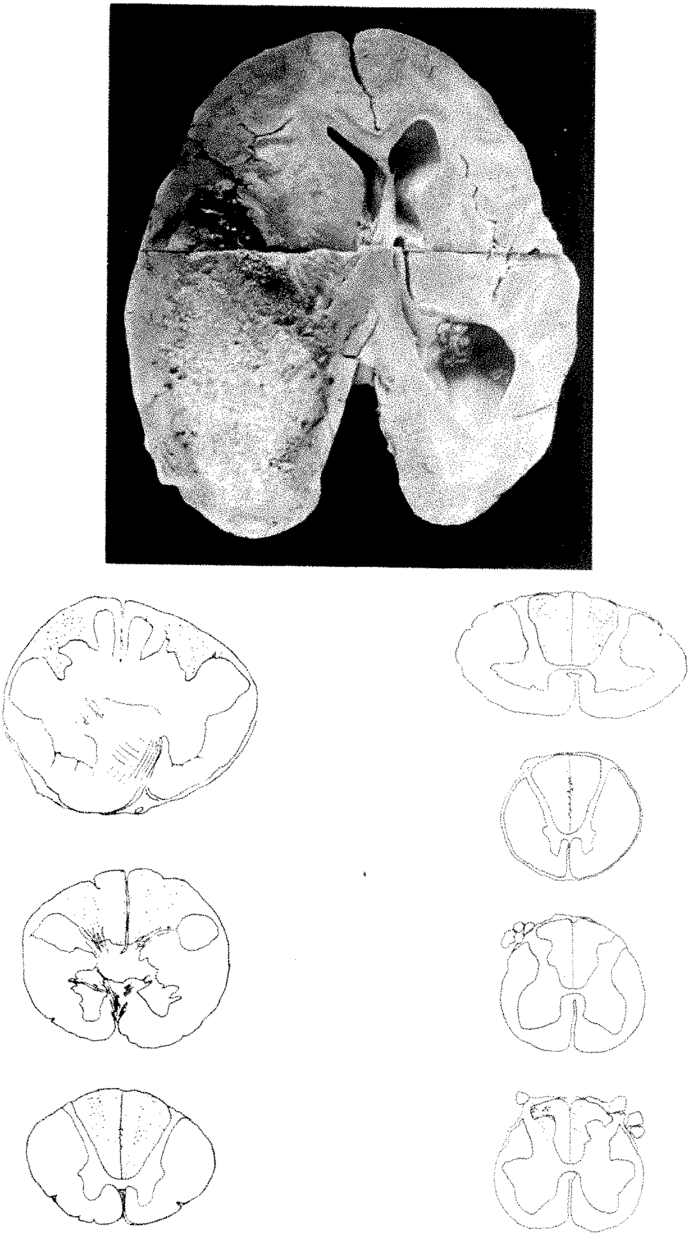


PLATE VIII.

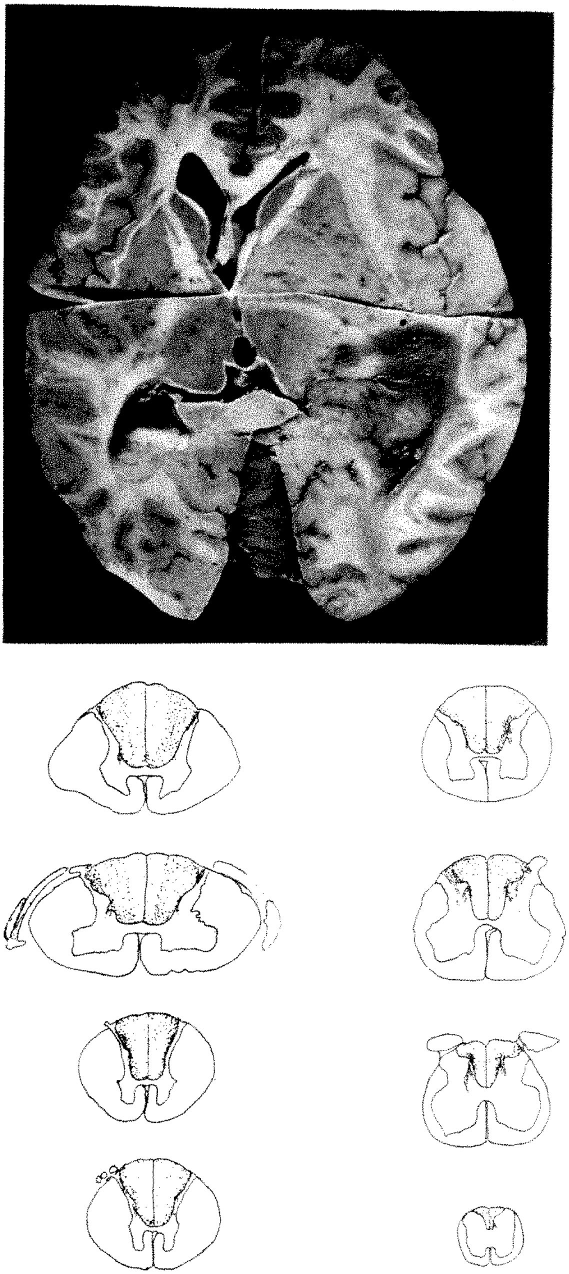


Case 9.

Tumour of the left temporo-sphenoidal lobe. (Mixed-celled sarcoma.)

The cord shows marked degeneration of the posterior columns from the sacral to the cervical region, being most marked in the postero-external columns of the lower cervical region.

PLATE IX.



Case 10.

Tumour of the right temporo-sphenoidal region. (Glioma.)

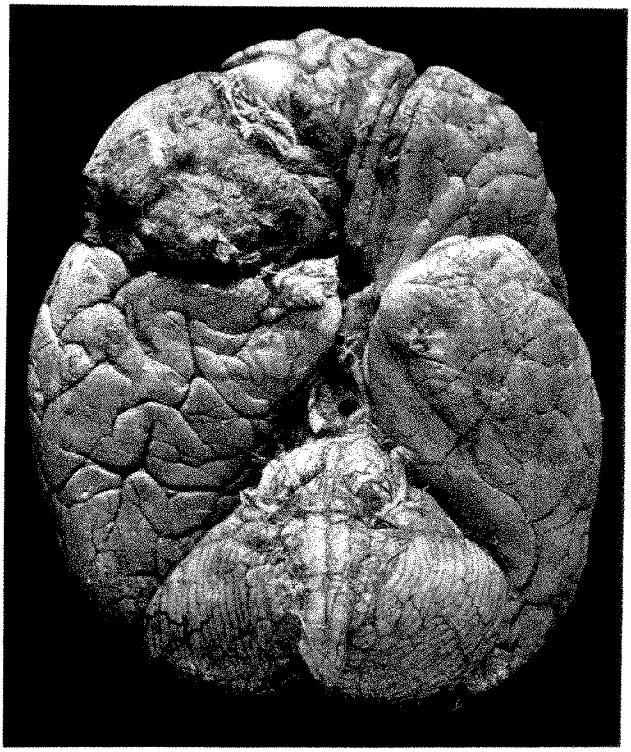
The cord shows marked degeneration from the sacral to the cervical region. In the cervical region the degeneration is most marked in the postero-external columns, while in the lumbar region it is evenly distributed throughout both.

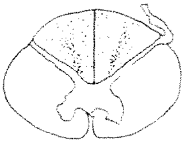
Case 11.

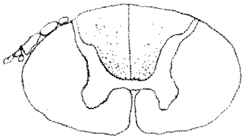
Tumour of the right temporo-sphenoidal region. (Spindle and round-celled sarcoma.)

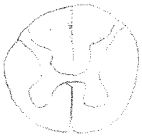
The cord shows marked degeneration from the sacral to the cervical region. In the cervical region the degeneration is most marked in the postero-external columns, while in the sacral region there is degeneration around the posterior median fissure arising probably from a lower sacral root, although occupying the region of the septo-marginal tract.

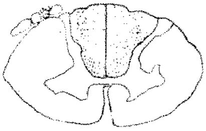
PLATE X.

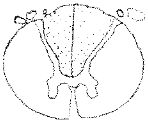


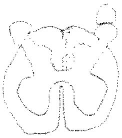


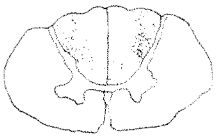


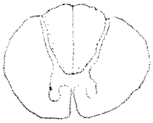












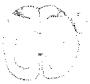
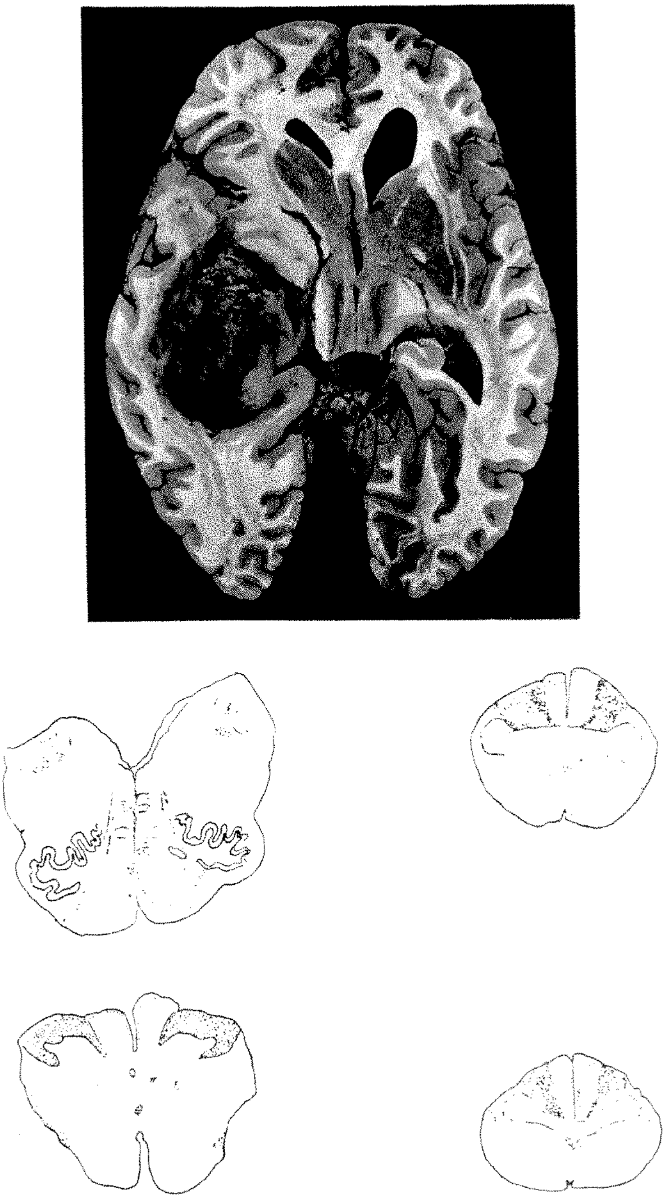


PLATE XI.



CASE 12.

Tumour of the right temporo-sphenoidal lobe. (Irregular-celled sarcoma.)
Photographed from the ventral surface.
The cord shows marked degeneration in the postero-external columns.

CASE 13.

Tumour of the left temporo-sphenoidal lobe. (Glioma.)

Only the upper portion of the tumour is shown.

There is degeneration in the posterior columns corresponding to the 4th and 5th right cervical roots, and this degeneration can be traced up to the funiculus cuneatus. There are a few degenerate fibres in the dorsal region of the cord and also in the crossed pyramidal tract of the right side.

PLATE XII.

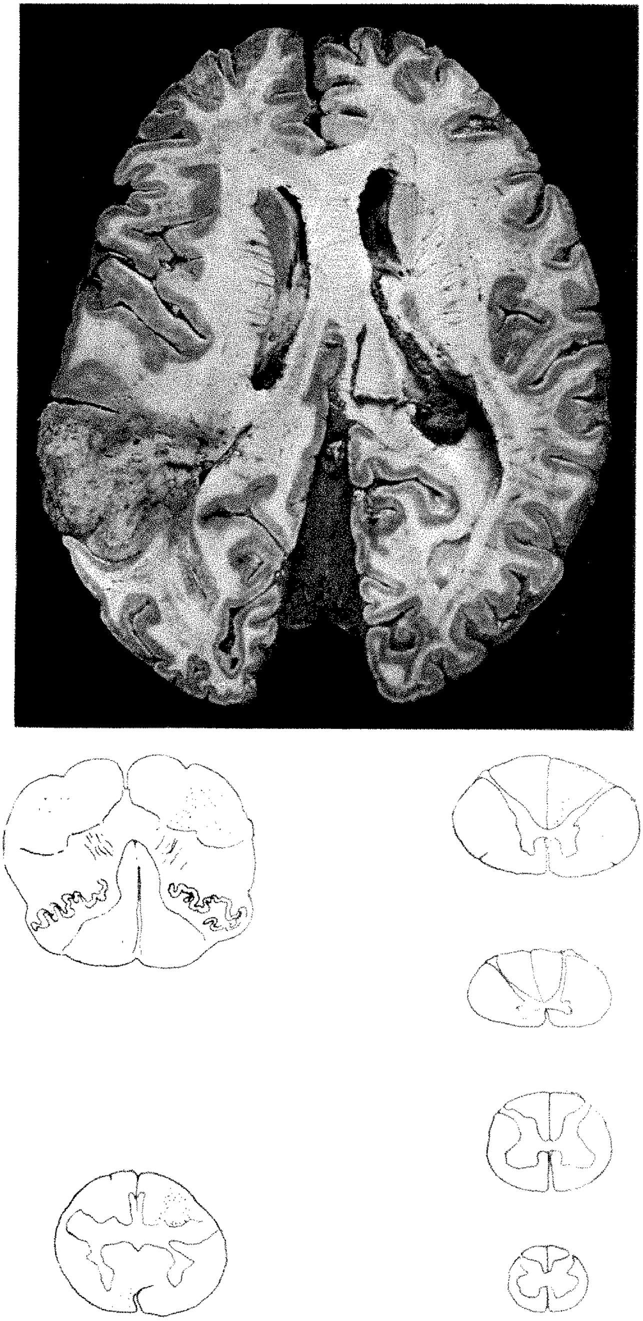
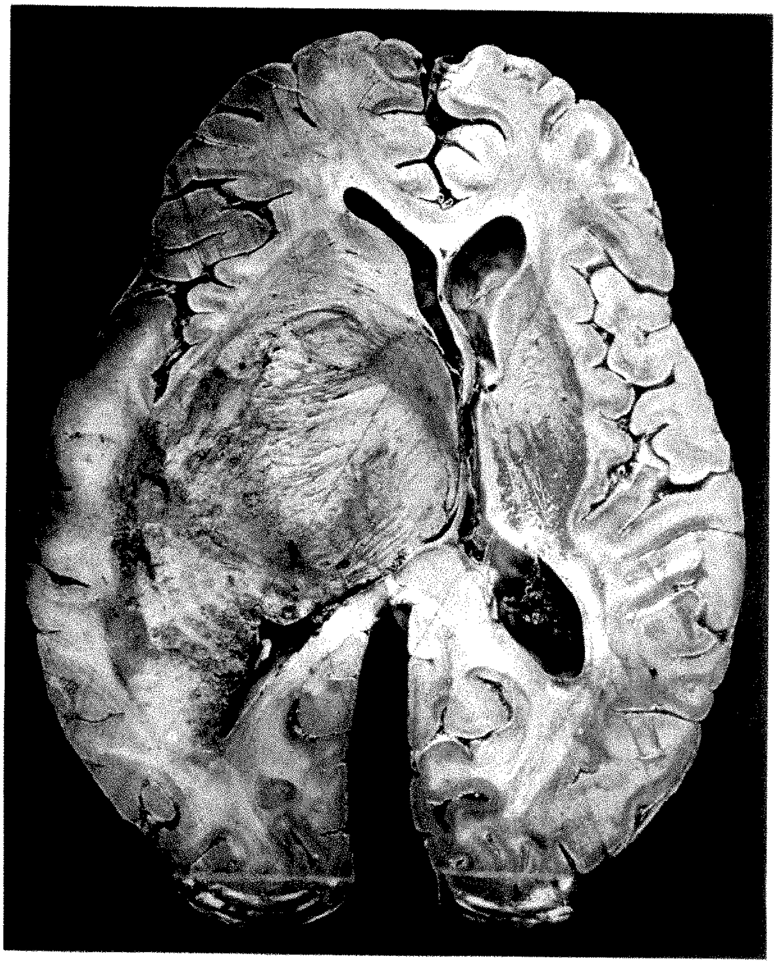


PLATE XIII.



CASE 14.

Tumour of the left cerebral hemisphere, involving the left temporo-sphenoidal lobe in its greatest extent. (Spindle-celled sarcoma.)

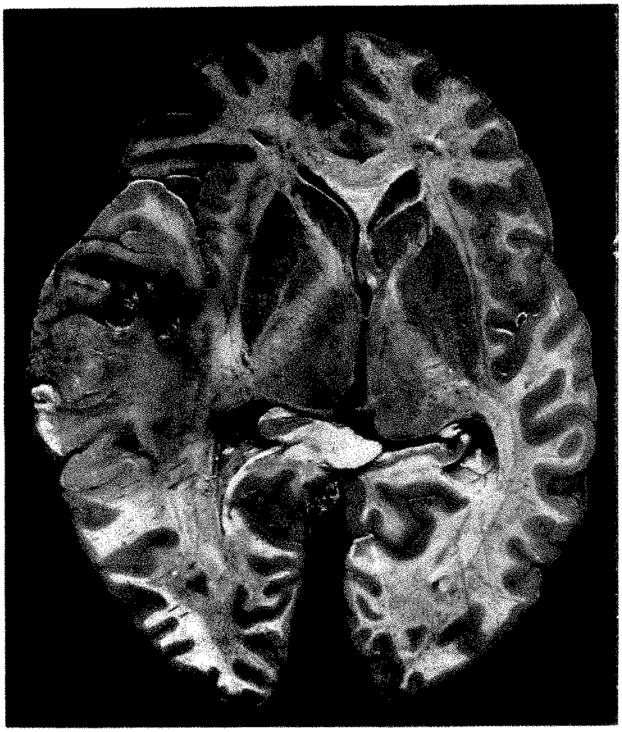
The cord shows no degeneration.

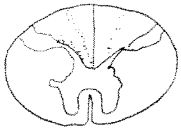
CASE 15.

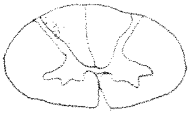
Tumour of the left temporo-sphenoidal lobe. (Mixed-celled sarcoma.)

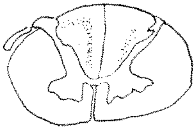
The cord shows degeneration of the right 6th and left 7th cervical roots, and these can be traced up to the funiculus cuneatus.

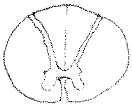
PLATE XIV.

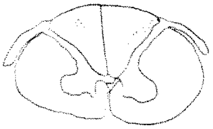












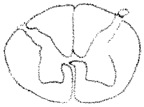
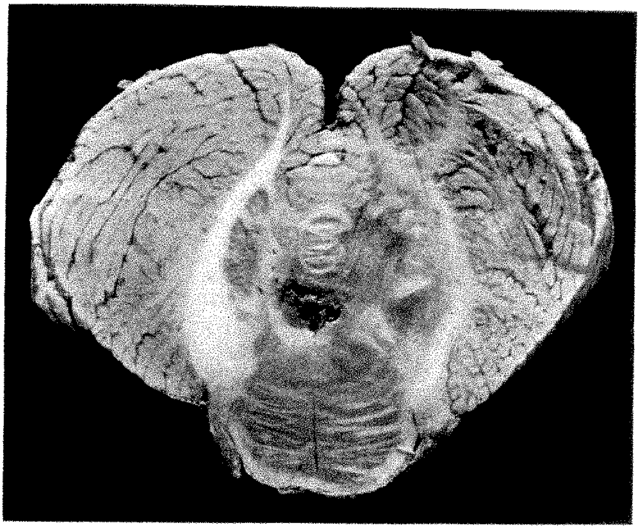


PLATE XV.

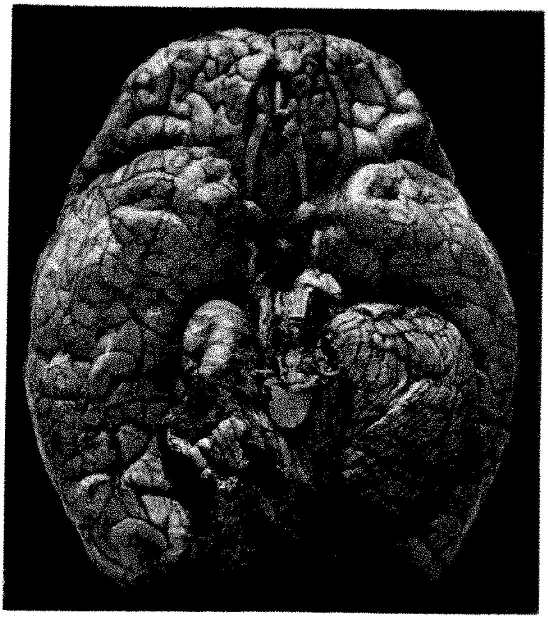


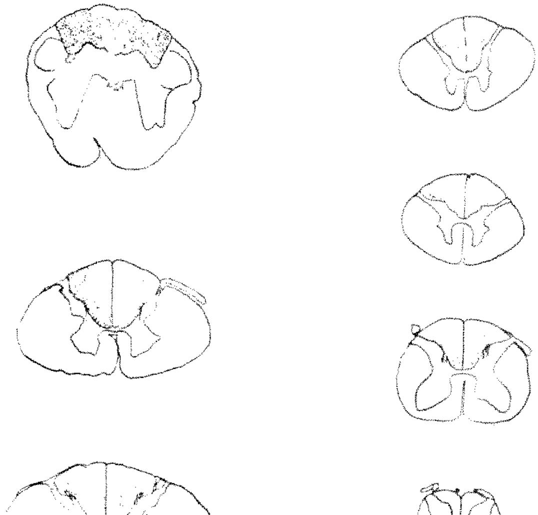
CASE 16.

Tumour of the left lobe of the cerebellum growing from the corpus dentatum and extending into the pons. (Infiltrating glioma.)

The cord appears perfectly normal.

PLATE XVI.



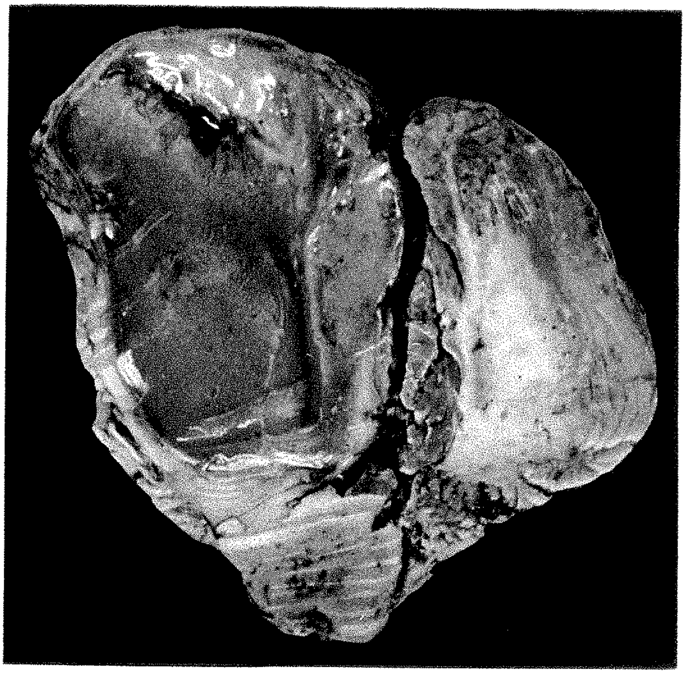


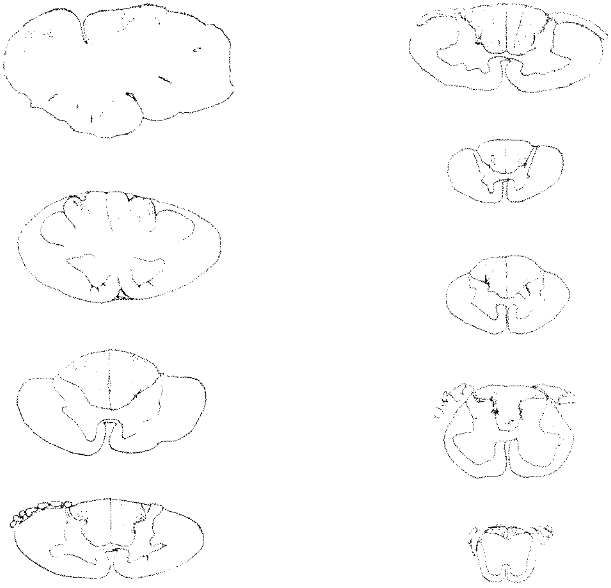
CASE 17.

Tumour of the right lobe of the cerebellum. (Fibro-sarcoma.)

In the cord there is marked degeneration of the postero-external columns in the cervical region, less degeneration in the dorsal and only a few scattered fibres in the lumbar region.

PLATE XVII.



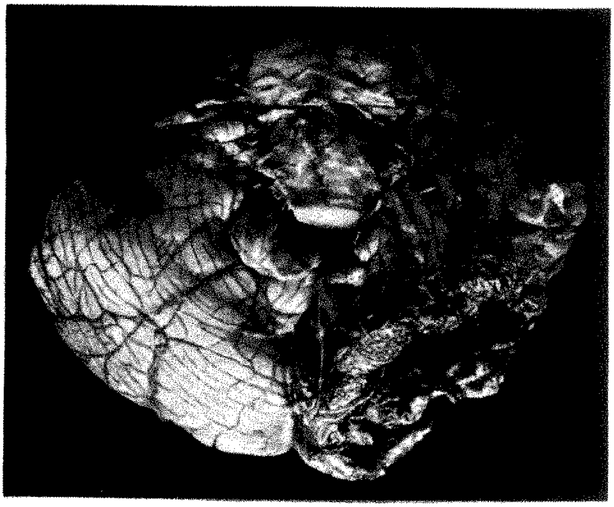


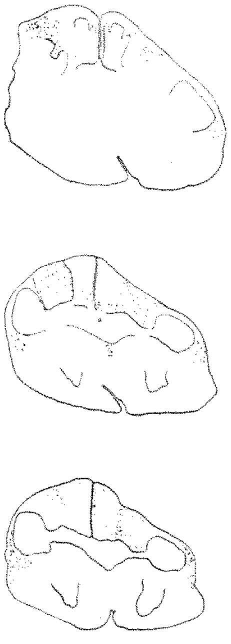
CASE 19.

Tumour of the left lobe of the cerebellum. (Glioma.)

The cord shows degeneration in the posterior columns from the cervical to the sacral region, being however most marked in the lower cervical region.

PLATE XVIII.

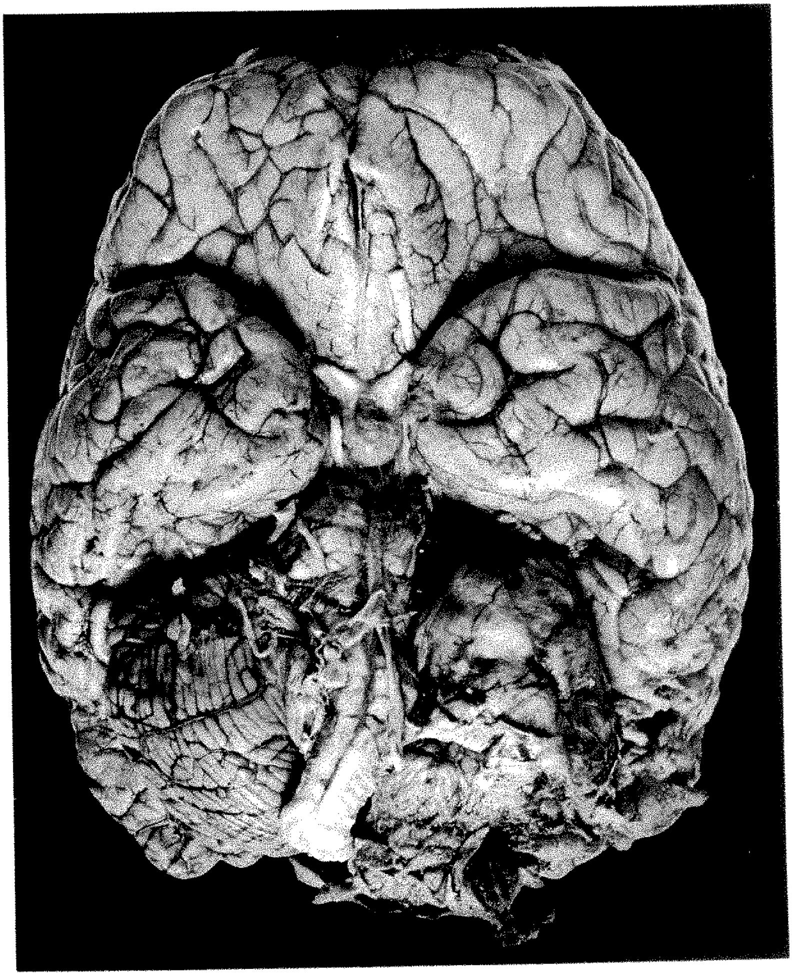




CASE 20

Tumour of the left lobe of the cerebellum. (Round-celled sarcoma.)
The upper portion of the cord shows degeneration of the posterior columns and of the direct cerebellar tract on both sides.

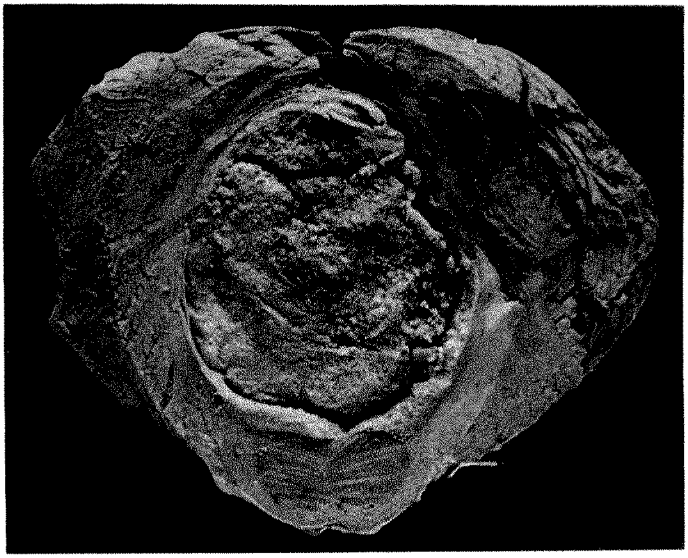
PLATE XIX.

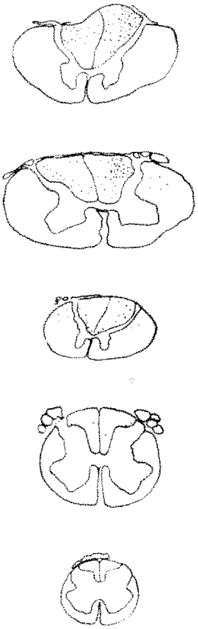


CASE 21.

Tumour of the left lobe of the cerebellum. (Fibro-sarcoma.)
The cord shows no degeneration.

PLATE XX.



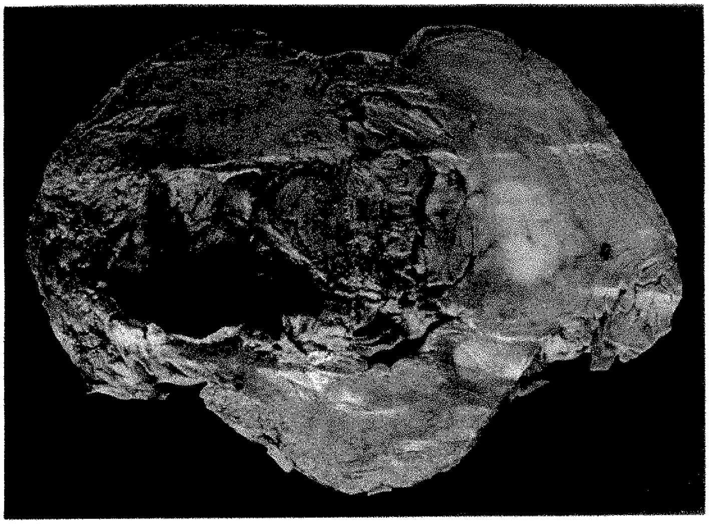


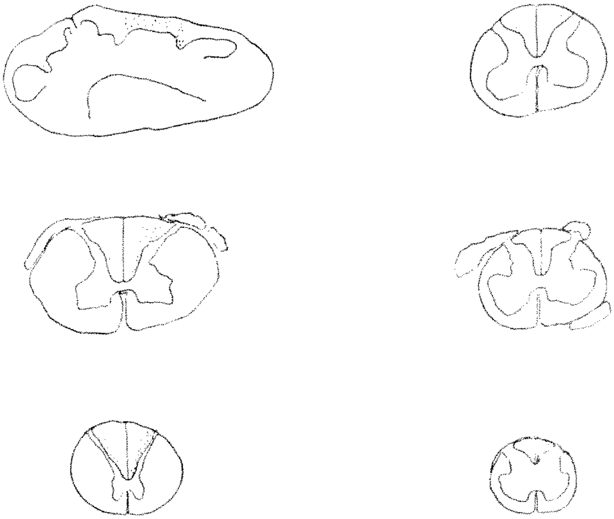
CASE 22.

Tumour of the middle lobe of the cerebellum. (Alveolar-sarcoma.)

The cord shows some degeneration of the posterior columns in the cervical region, less in the dorsal, and very little in the lumbar.

PLATE XXI.



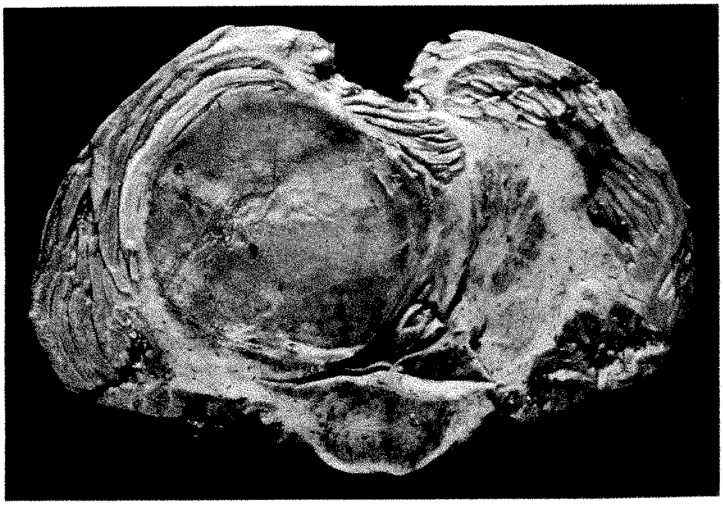


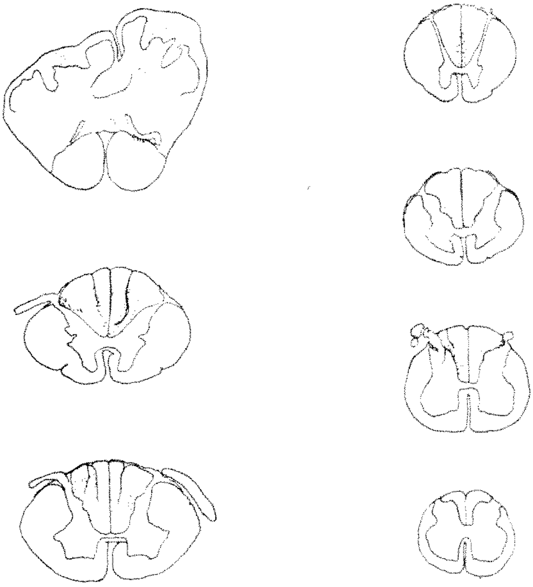
CASE 23.

Tumour of the right lobe of the cerebellum which has undergone cystic degeneration. (Glio-sarcoma.)

The cord shows slight degeneration of the posterior columns most marked in the cervical region.

PLATE XXII.



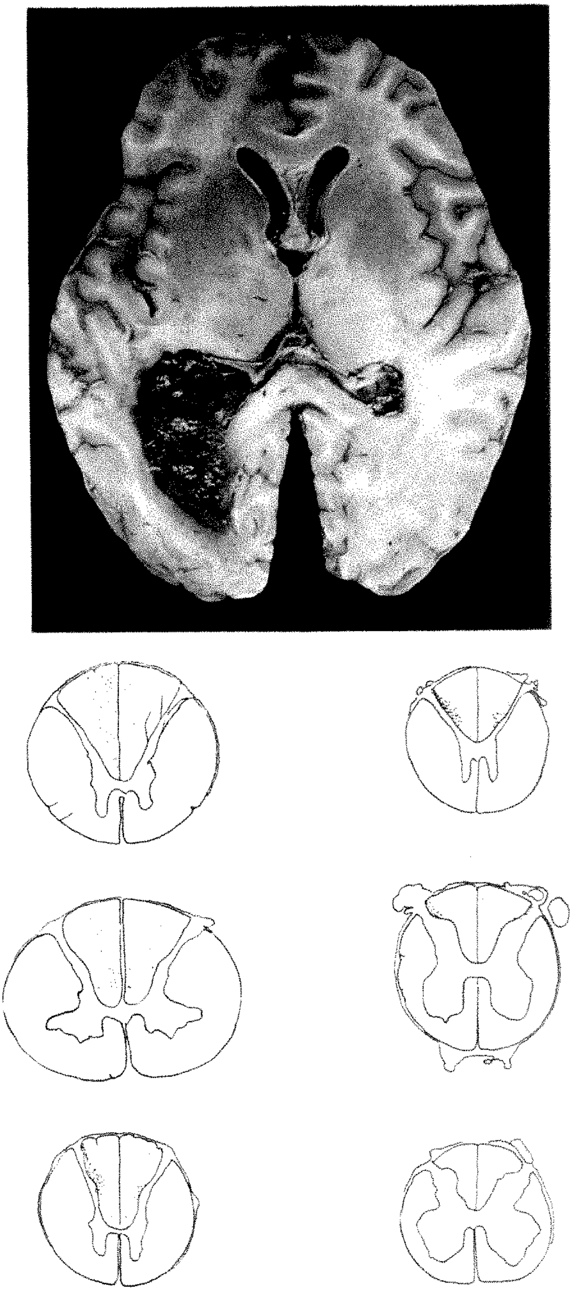


Case 24.

Tumour of the left lobe of the cerebellum. (Glioma.)

The cord shows slight degeneration of the posterior columns, most marked in the postero-external columns in the cervical region.

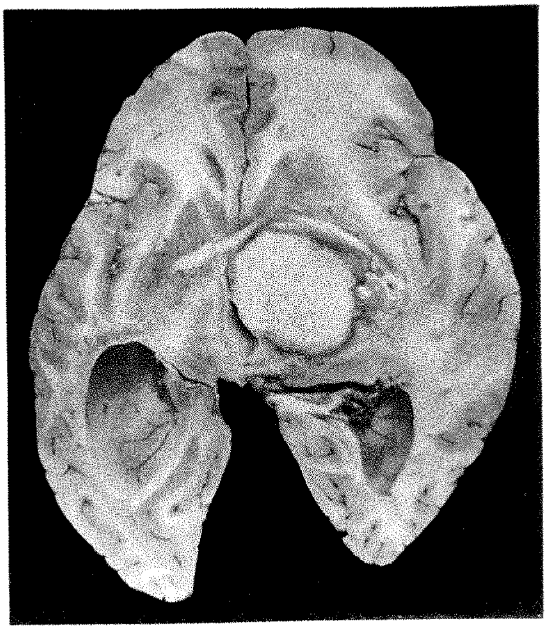
PLATE XXIII.

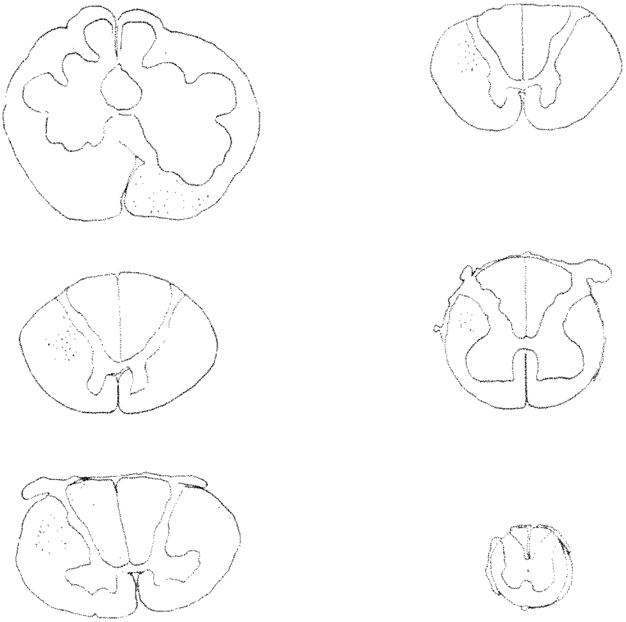


Case 25.

Tumour of the choroid plexus and left lateral ventricle. (Glio-sarcoma). The cord shows degeneration in the posterior columns in the lumbar, dorsal and cervical regions.

PLATE XXIV.



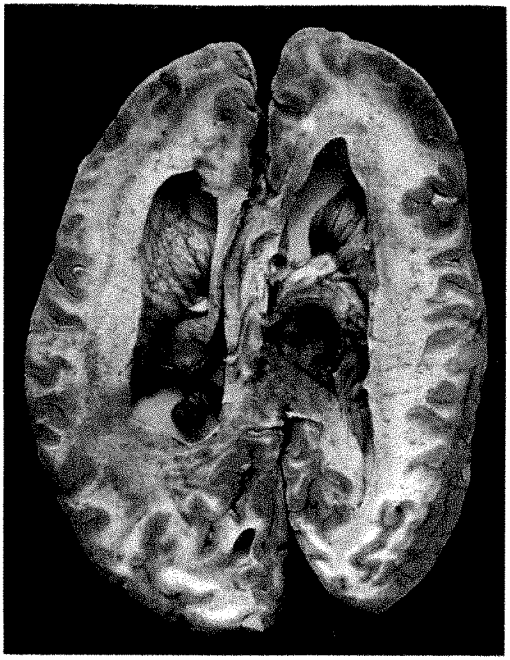


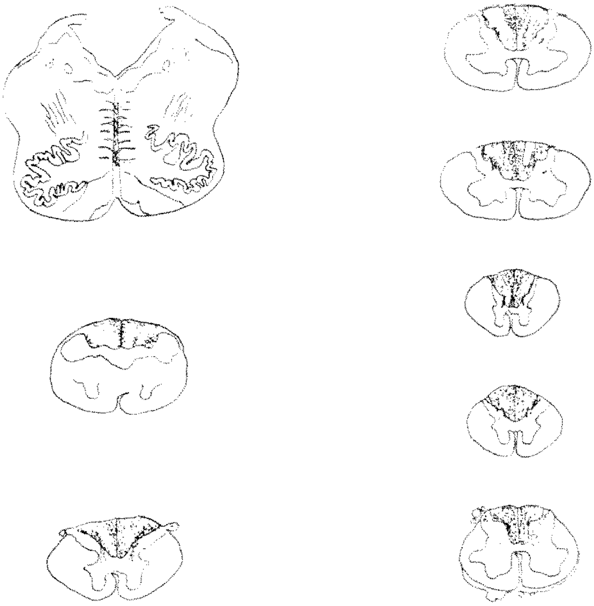
CASE 26.

Tumour of the right optic thalamus. (Tuberculous.)

The cord shows marked descending degeneration in the crossed pyramidal tract on the left side, and slight degeneration in the posterior columns in the cervical and dorsal regions.

PLATE XXV.



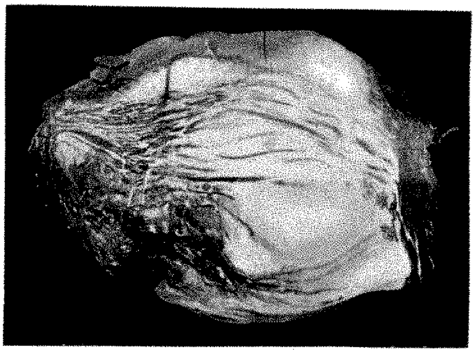


Case 27.

Tumour of the right optic thalamus and corpora quadrigemina. (Round-celled sarcoma.)

The cord shows marked degeneration of the posterior columns from the lumbar to the cervical region.

PLATE XXVI.

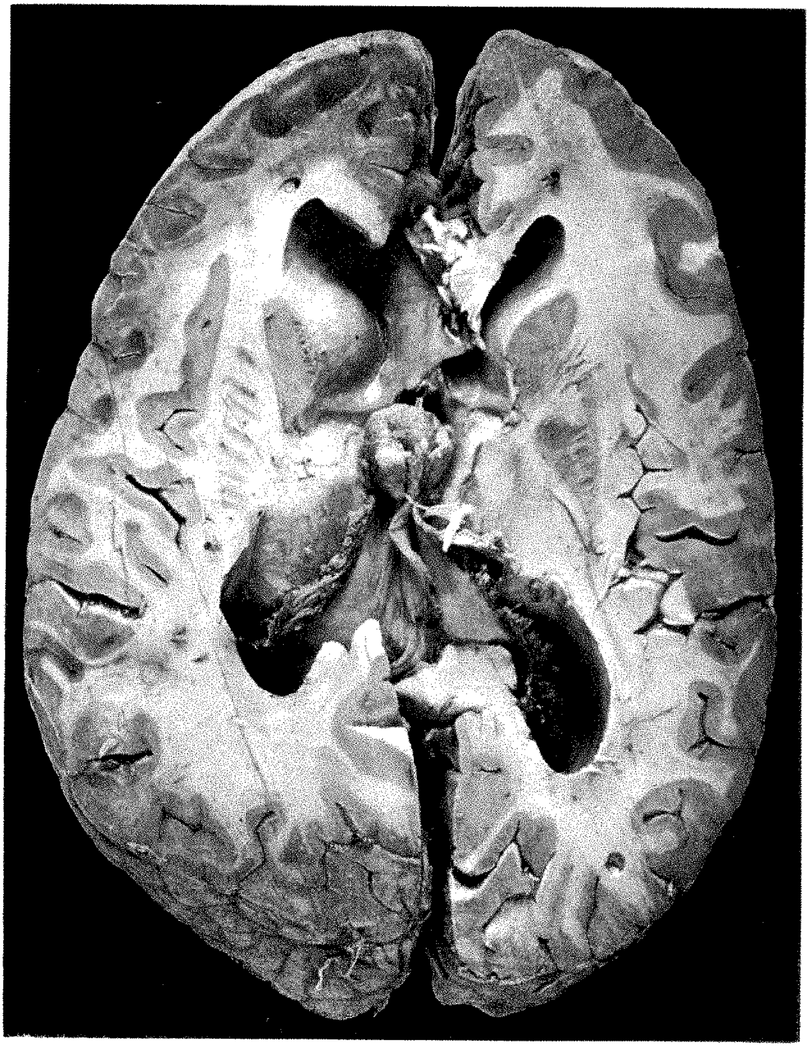


CASE 28.

Glioma of the pons. The photograph is taken from a transverse section through the pons stained by the Weigert-Pal method. The transverse fibres of the pons can be seen separated by the infiltrating growth.

The cord shows no degeneration.

PLATE XXVII.



CASE 29.

Cyst of the choroid plexus growing into the 3rd ventricle.
The cord shows no degeneration.

LIST OF PUBLISHED CASES.

Sex.	Age.	Situation of tumour.	Nature.	Duration.	Optic neuritis.	Knee-jerks.	Degeneration of posterior columns.	Degeneration of posterior roots.	Other degeneration.	Author.
F. 1894	33	L. cerebral hemisphere	Glioma	5 mths.	Present	Absent	Marked; cervical +	No degeneration	Cells of anterior horn	Mayer
M. 1894	46	Pressure on both frontal lobes	Endothelioma	12 mths.	Present	Absent	Marked; cervical +	None	None	Mayer
F. 1895	4	R. cerebral hemisphere	Spindle-celled sarcoma	7 mths.	Present	Absent	Marked; cervical +	Present	None	Dinkler
1890	—	L. lobe of cerebellum.	—	—	—	—	Marked	—	Ascending root of 5th L. cerebellar tract	Wollenber
F. 1894	62	Softening of L. cerebellar lobe	Softening	2 yrs.	—	—	Marked	—	L. pyramid	Campbell
M. 1894	73	L. lobe of cerebellum	Softening	?	—	Diminished	Marked; cervical +	—	L. sup. med. and inf. peduncle	Campbell
M. 1897	53	L. cerebral hemisphere	Spindle-celled sarcoma	5 mths.	None	Obtained	Marked; cervical +	Present	—	Ursin
M. 1897	60	L. occipital and R. frontal	—	5 mths.	Present	Active	Marked; cervical +	Present	—	Ursin
M. 1897	67	L. hemisphere	Cystic	4 mths.	Not examined	Active	Marked	None	Hypo-glossal on R. side	Ursin
M. 1896	47	L. hemisphere	Not stated	Over 2 mths., not def. stated	Present	Active R. > L.	Marked	Present	Pyramidal tracts Pyramid	Pick
M. 1896	50	R. hemisphere	Not stated	16 mths.	Active	K.-J. active	Marked; cervical +	—	—	Pick
C. 1896	5	Osteo-sarcoma of skull	Sarcoma	Not stated	Not stated	Not stated	Marked; cervical +	None	—	Pick
F. 1896	68	Both cerebral hemispheres	Glioma	Not stated	None	Active at first Diminished R. > L.	None	—	—	Pick
F. 1896	38	Diffuse cerebral sclerosis	—	11 mths.	Present	R. absent L. difficult	Marked; cervical +	None	—	Pick
F. 1896	16	3rd ventricle	—	18 mths.	Atrophy	Active	Marked; cervical +	None	Gowers' tract	Besold
F. 1896	11	Optic thalamus	—	3 yrs.	Atrophy	Active	Marked; cervical +	None	Gowers' tract	Besold
M. 1897	20	R. cerebral hemisphere	—	19 mths.	Present	Active	Marked	None	Left pyramid	Hoche
F. 1897	49	L. lobe of cerebellum	Glio-sarcoma	1 yr.	Present	Diminished	Marked; cervical +	None	—	Hoche
F. 1897	33	L. cerebral hemisphere	Fibro-sarcoma	3 mths.	None	Exaggerated	None	—	—	Hoche
M. 1899	19	Injury to R. cerebral hemisphere	—	20 days	—	—	Marked; cervical +	—	—	Bikeles

APPENDIX.

Table of Cases.

Frontal	1, 2, 3, 4, 5, 6
Parietal	7, 8
Temporo-sphenoidal	9, 10, 11, 12, 13, 14, 15
Cerebellar	16, 17, 18, 19, 20, 21, 22, 23, 24
Basal Ganglia and Pons	25, 26, 27, 28, 29

Case 1.—J. H., a lady's maid, aged 32 years, was admitted into the National Hospital under the care of Sir William Gowers, on July 15, 1898, complaining of headache, vomiting and dimness of sight. Her family history was unimportant. With the exception of some attacks of neuralgia in the forehead and two slight attacks of influenza, her health had always been excellent.

In March 1898, after an attack of sea-sickness, she first noticed severe headache "behind the eyes" and pain running down the back of the neck. The headache continued and increased in severity and she vomited daily for three months; the emesis bearing no relation to meals.

Two months later, she constantly saw double, and noticed that her sight was getting dim. No other symptom was complained of.

When admitted, she was healthy-looking and of very good intelligence. She stated that she was losing her memory, and that but for the headache and double vision she felt perfectly well.

Taste, smell and hearing were normal.

Vision $\frac{6}{6}$, J, with either eye. Visual fields and colour vision were good. Intense double optic neuritis with many hæmorrhages and much exudation.

Pupils normal. Weakness of right external rectus with corresponding diplopia.

Motion, gait, objective sensation, normal. Knee, wrist and elbow-jerks present and equal; plantars sluggish.

On June 19, on waking in the morning, she began to talk noisily and incoherently and had varied delusions. Face flushed, pupils dilated R. > L. No mental aberration had been present till this time. The delusions were present for three days.

On June 28 the following note was made: No delusions. Mental state normal. Pain much less. Visual fields markedly contracted. Weakness of both external recti. No other symptom had appeared, knee-jerks present.

July 7. She was much better. Mental state good. Headache slight. No fresh symptoms. She was sitting up and about the ward.

July 18. Much worse, no further symptoms. Mental state petulant and childish.

August 20. Much worse, and mentally heavy and dull. Knee-jerks present and equal. No further symptoms.

August 23. Difficulty of swallowing. She gradually became comatose, and died of respiratory failure.

Duration of symptoms five months.

Description of tumour (plate i.).—There was general flattening of the convolutions. The anterior portion of the falx was infiltrated by new growth and adherent to the superior frontal convolution. A large tumour was present in the left frontal lobe and was of a dark reddish colour with small dark areas within it. The growth was irregularly circular, and measured about 5 cm. in diameter, it had a sinuous outline and sharply defined limits except posteriorly where it merged into the normal brain tissue. The tumour had made its way across the middle line and was pressing on the inner border of the opposite hemisphere.

Microscopical examination (plate i.).—At the level of the corpora quadrigemina there was a small area of softening just at the outer angle of the fillet.

In a section taken through the middle of the pons, a bundle of degenerate fibres can be seen on the outer side of the fillet passing in a dorsal direction. There were some scattered degenerate fibres in the posterior longitudinal bundles, and in the pyramids.

At the level of the olive there was marked degeneration in both restiform bodies, and to a slight degree in both pyramids. The twelfth nerve was also degenerate on one side. The fibres of the fillet were practically free from any degeneration.

At the level of the posterior column nuclei there was marked degeneration in both the funiculus gracilis and cuneatus, and this was more marked in the latter than in the former. Marked degeneration was also present in the direct cerebellar tracts of both sides. The pyramids showed very little degeneration.

In the upper cervical region of the cord there was very marked degeneration in the postero-external and postero-internal columns of the cord and also in the direct cerebellar tract, but the pyramids showed very little degeneration. Below the level of the second cervical root there is very little degeneration in the direct cerebellar tract, but in its place there is a band of degenerate fibres lying between this tract and the pyramidal tract and this band extended forwards into the antero-lateral tract.

In the lower cervical region the degeneration in the posterior columns was still more marked, and that in the pyramidal tracts seemed rather to increase than diminish when traced downwards to the mid-dorsal region, but below this point the degeneration in the pyramidal tracts became progressively less marked.

In the lumbar region there was slight degeneration in the posterior columns and also in the crossed pyramidal tracts.

The degeneration extends into the posterior roots in the cervical region, but it is by no means so marked as that in the posterior columns.

By the Weigert-Pal method the cord appeared normal, and Clarke's column and Lissauer's tract were also normal.

Nature of growth.—The growth was composed of cells of varying shapes and sizes, some being triangular with a fine prolongation, and they were rather closely packed together—the prolongations of the cells forming a matrix in which the cells lay. The growth was not very vascular and in the portion cut seemed fairly uniform in structure (glio-sarcoma).

Case 2.—K. N., aged 44, was admitted into the National Hospital under the care of Dr. Beevor, on October 3, 1899.

The patient had complained of headache for six weeks, worse at night and paroxysmal in character, and he had vomited on one occasion. Three weeks before admission he went to a convalescent home and while there became dull and stupid, his eyesight began to fail and he staggered. He had fallen on two occasions hitting the left side of his head.

On admission he was very stupid, fatuous and very emotional. He could answer questions but not always correctly, and his articulation was very indistinct. He could name objects, but appeared unable to read printed or written words. He could write to dictation but could not copy nor could he read what he had written. Both optic discs showed intense optic neuritis. There was no loss of motor power or ataxy in the limbs or trunk, but the gait was unsteady and he tended to fall backwards and to the left. The knee-jerks were brisk and equal, and there was no ankle clonus. The arm-jerks were normal and equal, the plantar reflexes were lively and equal. Three days after admission he rapidly became comatose; the limbs became flaccid; the knee and arm-jerks could not be obtained and he died on October 6.

Description of tumour (plate ii.).—There was flattening of the convolutions, and situated in the left frontal was a tumour occupying the second and adjacent parts of the first and third frontal convolutions. The dura mater was adherent over its surface. On section an oval tumour measuring 6 cm. in the antero-postero diameter, and 5·5 cm. in the transverse direction, was seen reaching almost to the middle line, but not extending far enough back to affect the ascending frontal convolution.

Microscopical examination.—The cord appeared perfectly normal by the Marchi, Weigert-Pal and by the blue-black methods.

Nature of growth.—The growth was composed of large cells of irregular shape and size, among which were situated areas of a substance which took the stain badly, and in these regions the cells were broken up into a kind of *débris*. The growth was not vascular, and the coats of the vessels surrounding the growth were thickened. The appearance of the growth did not suggest a gumma but a mixed cells sarcoma undergoing degeneration. (Mixed celled sarcoma.)

Case 3.—B. K. was admitted to the National Hospital under the care of Dr. Bastian, on November 14, 1898. Two and a-half years previous to admission she suddenly fell down in the street and lost consciousness for a few minutes, and during the following fortnight she had two fits of a similar nature. Since that time she had had no more fits but had suffered from attacks of giddiness, for which she attended the out-patient department for eighteen months before admission. During the month of October, 1898, she was noticed to be mentally dull, and in the early part of November it was noticed that she used wrong words and complained of slight headache. On the morning of November 13 she was very drowsy, and on the following day was admitted to the hospital.

On admission the patient was found to be a well-nourished, healthy-looking girl. She lay in bed in a semi-comatose condition. There was complete paralysis of the right sixth nerve and nearly complete paralysis of the left sixth nerve. There was recent optic neuritis in both eyes. The left lower face did not move so well as the right. Motion and sensation in the trunk and limbs were natural. The knee-jerks were not exaggerated, the left being rather more easily obtained than the right. The elbow and wrist-jerks were brisk and equal. The plantar reflexes gave a flexor response. There was no aphasia. She rapidly became comatose and died seven days after admission. (The case was fully reported by Dr. Collier in the *Lancet*, March 25, 1899.)

Description of tumour.—The dura mater was adherent to the anterior part of the left temporo-sphenoidal lobe, the leptomeninges at the base of the brain showed considerable thickening and there was recent meningitis over the posterior extremities of the second and third left frontal convolutions. A growth was found involving the inferior margin of the second left frontal convolution, and the whole of the posterior part of the third left frontal convolution and also the anterior part of the first left temporo-sphenoidal convolution. The growth measured 3·7 by 3 cm.

Microscopical examination of the cord.—The cord appeared perfectly normal by the Marchi and Weigert-Pal methods. No degeneration was present in the posterior roots.

Nature of growth.—The growth was composed of small round cells staining deeply, and areas evidently undergoing degeneration in which little or no structure was visible. There were rounded areas with definite walls filled with what appeared to be young fibrous tissue, and some of these contained badly formed giant cells. They were probably thrombosed vessels in which organisation of the clot has taken place. The walls of the vessels were very much thickened. (Gumma.)

Case 4.—L. L., a servant, aged 17 years, was admitted into the National Hospital under the care of Dr. Hughlings Jackson, on January 12, 1899. When in apparent good health in July, 1898, she had a fit commencing in both hands, consciousness being lost late. A week later a similar fit occurred. In August, 1898, severe headache and vomiting set in. These symptoms improved greatly under treatment with mercury and iodide of potassium.

On admission she was intelligent and her memory was good. Vision $\frac{6}{60}$ badly, and Jaeger 4 with either eye. Intense double optic neuritis. Marked spontaneous nystagmus increased on lateral deviation.

Cranial nerves, motion, gait, sensation and sphincters were normal. Knee, wrist, and elbow jerks were present and equal. She began to develop slight signs of mental weakness, but no other signs appeared up till the time of her death, from a sudden attack of coma, on June 28, 1898.

Duration of symptoms, eleven months.

Description of tumour (plate iii.).—On the inner side of the skull, situated over the centre of the tumour was an exostosis of pyramidal shape, which had caused a depression in the dura mater. There was some flattening of the convolutions, and the dura mater was firmly adherent over a large tumour situated in the right hemisphere extending from the middle line and involving the superior and middle frontal convolutions in their posterior part. The greater portion of the tumour lay anterior to the ascending frontal convolution, but one small nodule extended into it. A vertical section made through the tumour showed that it extended deeply into the cerebral substance. The corpus callosum was pushed downwards and the tumour bulged into the longitudinal fissure, causing a depression in the opposite hemisphere. The lateral ventricle of the right side was pressed upon, but there was no distention of either ventricle. The fibres of the internal capsule had escaped direct involvement by the tumour.

Microscopical examination (plate iii.).—By the Marchi method there was practically no degeneration in the sacral, lumbar and lower dorsal region of the cord. In the upper dorsal region there was slight degeneration, which increased in the cervical region. The degeneration was almost entirely confined to the postero-external column, and could be traced up to the nucleus cuneatus, where it ceased and sections above this level showed no degeneration.

By the Weigert-Pal method the cord appeared perfectly normal, and by the Nissl method no abnormality could be detected either in the cells of the anterior horn or of Clarke's column.

Nature of tumour.—The tumour was composed of spindle cells with large nuclei and these cells had an irregular alveolar arrangement, numerous cell nests being scattered irregularly throughout. The growth was a psammoma.

Case 5.—J. T., a compositor, aged 32 years, was admitted into the National Hospital under the care of Dr. Bastian, on December 5, 1898. Jacksonian attacks of the right face had been present for ten years. In May, 1898, an attack of left sided convulsions followed by transient left hemiplegia, occurred. Frequent left sided attacks then followed and he gradually became hemiplegic on the left side and also weak on the right side. Some slight headache had been present for a year.

On admission the condition was as follows:—Mental state intelligent. Optic neuritis of long standing. Marked left hemiplegia (leg and foot most affected). Slight right hemiplegia (leg and foot most affected). Trunk muscles very weak. No anæsthesia. Knee, wrist and elbow jerks present. L. > R. Left foot clonus. There was a large hard swelling about the size of an egg, and continuous with the skull, most prominent at about the middle of the sagittal suture, and tender to hard pressure.

He had Jacksonian attacks, beginning sometimes in the left foot and sometimes in the muscles of the left side of the abdomen. Later on he had similar attacks beginning in the right foot.

An operation was performed, and a large amount of growth was removed, but the tumour which was situated in the great longitudinal fissure was too extensive for extirpation. He died on February 18, 1899.

Duration of symptoms: epilepsy ten years; hemiplegia ten months.

Description of tumour (plate iv.).—A large opening was present in the skull, extending across the middle line of the vertex, this portion of the calvarium having been removed at the time of operation. The longitudinal sinus was blocked by a mass of growth. On the right side of the brain there was a large softened area corresponding to the tumour removed, and on the opposite side close to the middle line was another mass of growth evidently of the same nature. The dura mater was adherent to the brain around the edges of the wound. A transverse section was made across the brain and this showed a large tumour involving and growing from the dura mater extending for 4 cm. into the left hemisphere immediately to the left of the longitudinal fissure. On the right side the growth did not extend so deeply, being only about 3 cm. from the surface (a large portion of the growth had been removed from this situation by operation). The growth was firm and hard, and was not very vascular. It was definitely limited and did not infiltrate the brain. The growth measured 13 cm. in longitudinal direction, 8 cm. in a transverse direction, and 4 cm. in its greatest depth, and involved both the frontal and parietal lobes.

Microscopical examination (plate iv.).—By the Marchi method the cord and medulla showed descending degeneration in the crossed pyramidal tracts of both sides, and also in the direct pyramidal tract, but this was more marked on the left side than the right; the degeneration could be traced down to the lumbar region. There was no posterior degeneration in the cord below the level of the second cervical roots, but at this level two degenerate roots could be seen entering the cord. In the segment above this there was marked degeneration both in Goll's column and Burdach's column, and this could be traced up to the medulla. From the affection of both tracts it would seem probable that damage to the cervical cord was wider than indicated by the section at that level. Degeneration of the anterior roots also was present at that level. Some degenerate fibres were present in the raphe in the upper portion of the medulla.

By the Weigert-Pal method the posterior columns of the cord at the level of the second cervical were very pale, but no change could be found in the lower portion of the cord. When stained by aniline blue black, the cells of the anterior horn and of Clarke's column appeared normal. At the level of the second cervical there was an increase of fibrous tissue around the posterior fissure, but not affecting so wide an area as that shown by the Weigert-Pal method.

Nature of growth.—The tumour consists of spindle cells with large nuclei and irregular and indefinite alveoli. (Alveolar sarcoma.)

Case 6.—J. W., aged 26, was admitted into the National Hospital under the care of Dr. Ormerod, on August 15, 1899.

For the two years previous to admission, the patient had suffered from fits followed by attacks of vomiting, and for the last thirteen months of this period he had had otorrhœa. He had had syphilis two to three years ago. He attributed his illness to a blow on the ear two and a-half years ago, but he said that he had been deaf previously to this.

On admission he was a big muscular man with a defective memory and a confused mental state. There was extreme double optic neuritis. Hearing was defective in the left ear. He could only stand with difficulty, and tended to fall to the left and backwards when his eyes were closed, but he could, however, walk fairly straight. He was a left-handed man. All movements were well performed, but the right hand was stronger than the left. Sensation was normal. Reflexes: The elbow jerks were increased. The knee-jerks were increased and the right was somewhat greater than the left. There was no ankle clonus, and the plantars gave a flexor response. There was some tenderness over the left mastoid. The temperature was subnormal. The patient was trephined over the left temporo-sphenoidal lobe, but nothing was found, and he died on the following day.

Description of tumour (plate v.).—There was an opening in the skull over the left temporo-sphenoidal lobe. The convolutions were flattened. There was considerable destruction of the left temporo-sphenoidal lobe due to the operation. The right superior frontal convolution was broad and flattened, and on palpation felt hard, and it was obvious that a large tumour occupied the right frontal region, and it could be seen bulging into the longitudinal fissure and compressing the cerebral hemisphere of the opposite side. On section, a cystic tumour containing yellowish gelatinous material was found to occupy the right frontal region. The tumour measured 5 × 5 cm., and appeared to have a fairly definite margin. Besides a large cyst there existed numerous smaller ones situated in the peripheral portion of the growth. The growth extended across the middle line and lay between the corpus striatum and the corpus callosum. The basal ganglia on the right side were pressed backwards. The grey matter of the cortex in the frontal region was very thin and presented no clear line of demarcation from the white matter.

On careful inspection of the spinal cord it was seen that the fifth left lumbar root was grey and thin as compared with the corresponding root on the other side. No other root appeared to have been affected.

Microscopical examination (plate v.).—By the Marchi method there was degeneration of the fifth left lumbar root and the degenerate fibres from this could be seen at the level of the third lumbar root. The number of degenerate fibres, as seen by this method, was comparatively small when compared with the marked degeneration as shown by the Weigert-Pal method.

The degeneration could be distinctly traced up to the mid-dorsal region, above which, however, it becomes very little marked, while at the level of the second cervical root there was practically no degeneration. There was no degeneration in the funiculus gracilis and cuneatus.

Weigert-Pal. By this method the degeneration of the fifth left lumbar root was well seen, and a band of degeneration could also be seen at the level of the third sacral. The lower segments however, showed no change. In the mid-dorsal region the column of Goll was distinctly paler on the left side than the right, but both the columns of Goll are paler than the columns of Burdach. In the cervical region the same condition was present, and the same change could be seen in the funiculus gracilis. No distinct change could be detected in Lissauer's tract.

By the Nissl method the cells of the anterior horn and of Clarke's column appeared normal. At the level of the third lumbar root the cells were fewer on the left side than the right, but this condition was not striking.

An increase in the glia tissue about the degenerate root could also be seen by this method.

Nature of growth.—The growth was composed of a loose meshwork with irregular nuclei scattered sparsely throughout its substance. There were large areas of but slightly stained tissue, often surrounded by nuclei. These were probably portions of the tumour undergoing hyaline degeneration, as they closely resembled the hyaline tissue seen in the most degenerate portion of the tumour. (Glioma.)

Case 7.—W. S., aged 30, a dairyman, admitted into the National Hospital under the care of Dr. Beevor on July 18, 1898. He had been suffering from Jacksonian attacks in the left arm and face with progressive brachio-facial monoplegia for eleven months; headache and vomiting seven months; mental derangement two months.

On admission he was drowsy and delirious. Moderate double optic neuritis. Conjugate deviation to right. Marked brachio-facial monoplegia of left side. Left leg slightly weak. Anæsthesia of cortical type in left upper limb. Intense pain and great tenderness immediately above the right ear. Wrist and elbow-jerks L. > R.; knee-jerks brisk L. > R.; left foot clonus.

On July 24, Mr. Horsley removed a large tumour from the right motor area. The wound healed by first intention. The patient became maniacal and died suddenly on August 29.

Duration of symptoms twelve months.

Description of tumour (plate vi.).—There was an opening into the skull on the right side, and a large gap in the cortex of the same side, measuring about 8·5 cm. across; inferiorly, it involved the superior temporal and hinder part of middle temporal convolutions. A horizontal section into the hemisphere showed that the external capsule and the outer part of the lenticular nucleus had been removed, but that the internal capsule had itself escaped in its entire extent.

Microscopical examination (plate vi.).—Marchi's method showed recent well-marked degeneration in the right pyramid, above the decussation and in the corresponding direct and crossed pyramid below that point. No degeneration was present in the posterior columns. By the Weigert-Pal method the cord appears perfectly normal.

Growth not examined.

Case 8.—R. B., aged 32, was admitted to the National Hospital, under the care of Dr. Tooth, on December 10, 1897.

Two months before admission he had had a fit, commencing in the left great toe, spreading to the hip; this lasted ten minutes, the arm being unaffected. There was no loss of consciousness. On the following day the patient had had two similar attacks, in the second of which he lost consciousness. The fits have recurred every seven to ten days. After the third fit there was weakness of the left arm and leg. Headache had been present for two to three weeks, but there had been no vomiting.

On admission there was optic neuritis, weakness of the left side of the body, and slight left hemianæsthesia. The left knee-jerk was greater than the right; there was ankle-clonus on the left side. The optic neuritis and the weakness increased, and in February Mr. Horsley removed a large tumour from the right motor cortex. In April he could walk with assistance, and went home for a time. He returned again in June, with a hernia cerebri, and the wound was again opened up. He died about a month later, the hernia still pressing through the opening in the skull.

Description of tumour (plate vii.).—A large opening was present in the skull on the right side, the result of the operation. Through this opening a large fungating mass of brain substance protruded; the convolutions were much flattened. The right crus was much flattened and diffluent. The cerebellum and pons were normal. The brain was cut by transverse section, and a large tumour, measuring 9 cm. in the antero-posterior diameter, by 7 cm. in the lateral diameter, was seen to occupy the whole of the middle third of the right hemisphere. The tumour extended from the surface to the longitudinal fissure, and involved the falx cerebri and the hemisphere of the opposite side to a slight degree. The tumour was firm, hard, and white in appearance, with numerous irregular cavities situated throughout its substance. The margins of the tumour were fairly clearly defined.

Microscopical examination (plate vii.).—By the Weigert-Pal method, sections of the medulla and spinal cord showed very marked degeneration in the left crossed and the right direct pyramidal tract; the degeneration extended down to the lumbar region; no degeneration could be seen in the opposite pyramid by this method. By the Marchi method, the most marked degeneration was in the crossed pyramidal tract of the right side, *i.e.*, on the opposite side to the most marked degeneration, as shown by the Weigert-Pal method. There were a few degenerate fibres on the left side and also in the posterior columns; such degeneration being scattered and rather more marked in the cervical than in the dorsal or lumbar regions.

Nature of growth.—The growth was composed of cells of varying size and shape, among which strands of newly-formed connective tissue could be seen. Towards the margin of the tumour this merged into dense and well-formed fibrous covering, resembling the structure of the dura mater. (Mixed cell sarcoma.)

Case 9.—L. G., aged 15 years, was admitted into the National Hospital, under the care of Dr. Beevor, on July 11, 1898. The family history was unimportant. Her health, up till the commencement of this illness, had always been good. In December, 1897, she began to vomit daily. In March, 1898, severe vertical headache first occurred and persisted, and she had diplopia. In June, 1898, she gradually became completely blind.

When admitted she was a healthy-looking child, and was able to get about. Intelligence good. No fits. Vision reduced to slight perception of strong light. Intense double optic neuritis becoming atrophic. Slight nerve deafness in right ear. The cranial nerves, limbs, trunk, sensation, and sphincters were normal. Gait normal. Knee, wrist, and elbow-jerks present and equal. On July 12 the knee-jerks could only be obtained with reinforcement. On August 1 the left knee-jerk was absent, as were the wrist and elbow-jerks. The right knee-jerk was a mere flicker. After this time she constantly complained of severe aching pain in the legs, from the knees down. The knee-jerks remained absent, but on a few occasions a trace of the right knee-jerk was obtained by reinforcement. On August 20 nystagmus and slight right facial weakness were noticed. The pains in the legs were troublesome, and came on in sharp twinges. No further localising signs appeared. She became comatose, and died on October 13.

Duration of symptoms ten months.

Description of tumour (plate viii.).—The convolutions were flattened and a small cystic projection was noticed on the inner border of the lower surface of the left temporo-sphenoidal lobe which proved on further examination to be the dilated horn of the lateral ventricle. After hardening in formalin, a horizontal section was made through the cerebral hemispheres so as to expose the capsule. The left hemisphere was seen to be occupied by a very large growth which extended from the tip of the occipital lobe to about 5 cm. from the tip of the frontal lobe. There was a hæmorrhage situated in the anterior portion of the growth.

The growth was yellowish grey in colour with a few punctiform hæmorrhages and measured 12 cm. by 6 cm. The right lateral ventricle was dilated. The examination of the other organs was negative.

Microscopical examination (plate viii.).—By the Marchi method, there was marked degeneration in both the postero-external and internal columns in the lumbar region. In the dorsal region the degeneration was most marked in the cornu commissural zone, while in the cervical region the degeneration was most marked in Burdach's column, and could be traced up to the funiculus gracilis and cuneatus, where it was evenly distributed throughout both bundles. The direct cerebellar tract showed no degeneration. The other tracts of the cord appeared normal though there were perhaps one or two degenerate fibres in one pyramid. No degeneration could be traced above the posterior column nuclei. The posterior nerve-roots showed well-marked degeneration, and the degeneration was most marked in the eighth cervical and first dorsal.

By the Weigert-Pal method the cord appeared perfectly normal, and by the blue-black method the cells of the anterior horn appeared normal. Clarke's column and Lissauer's tract also appeared normal.

Nature of growth.—The growth was composed of irregular spindle-shaped cells, with small areas undergoing hyaline degeneration. Other areas had undergone a caseous degeneration and it was only at the outer margin of the tumour that the true nature of the growth was visible. (Mixed celled sarcoma.)

Case 10.—A. S., aged 12, was admitted on September 22, 1898, into the National Hospital, under the care of Dr. Buzzard.

Four months before admission, after an attack of influenza, she began to have frequent attacks of *petit mal.* She would suddenly turn pale and look strange, and say "I feel so funny." A fortnight later it was noticed that in some of the attacks the left arm twitched.

She was sent to the Meath Home for Epileptics, and when admitted there she was constantly falling asleep at all times of the day, though quite bright and natural when awake. It was then noticed that she did not use the left side of her face in talking so well as the right.

A month before admission her sight began to fail rapidly. A fortnight later paroxysms of vomiting began for the first time in her illness. She had had no headache until two days before admission. On admission she was obviously very ill. Her mental state was intelligent. Speech and articulation were normal. She had frequent Jacksonian attacks, beginning sometimes in the left face, sometimes in the right face, sometimes in the right hand and sometimes in the left hand, remaining always confined to the side on which the attack commenced. She was quite conscious and able to speak during the attacks. Taste, smell and hearing were normal. There was intense optic neuritis showing a commencing subsidence into atrophy. There was absolutely no light perception. There was complete palsy of the right third and sixth nerves, and partial palsy of the left third and sixth nerves. There was very slight weakness of the left lower face and of the left arm. There was absolutely no weakness of the legs, and her gait was natural. There was no localised cranial pain or tenderness. Sensation was natural. The knee, wrist and elbow-jerks were absent and were never obtained up till her death. The plantar reflex on the right side gave a marked flexor response, that on the left side a vigorous extensor response. This condition of the plantar reflex persisted till the day before death, two months later, when she became deeply comatose, and the extensor response was present on both sides, but was much more marked on the left side.

A month after her admission she dragged the left foot slightly in walking, but after this the hemiplegia did not progress.

For six weeks after admission the clinical aspect of the case did not alter. She was up and about the ward. She did not suffer much pain, and her mental state was intelligent. She was never ataxic. A fortnight before death she gradually became drowsy and from that time slowly sank into coma.

Duration of symptoms six months.

Description of tumour (plate ix.).—The brain showed marked flattening of the convolutions, and the under surface of the right temporo-sphenoidal lobe was seen to be the seat of new growth. The lobe was swollen and enlarged transversely. On section the right temporo-sphenoidal lobe was found to be infiltrated by new growth and the descending horn of the lateral ventricle was filled by it. There was some dilatation of the lateral ventricle on the left side.

Microscopical examination (plate ix.).—By the Marchi method, sections of the cord taken from the cervical, dorsal and lumbar regions showed well-marked recent degeneration in both posterior columns, and it was almost as marked in the lumbar as in the cervical region. In the dorsal region the degeneration was most marked around the incoming roots, and in the lower and upper cervical the degeneration was more marked in the columns of Burdach than in the column of Goll, though the degeneration was considerable in the latter column. The degeneration could be traced up to the level of the second cervical root (the cord was not available above this level). No degeneration could be found in the direct cerebellar tract. Some of the degenerate fibres that pass in by the posterior roots could be traced into the base of the posterior horns and ramifying there became lost among the cells of Clarke's column and also of the cells of the anterior horns. Posterior nerve roots: The posterior roots from the cervical, dorsal, and lumbar region all showed well-marked recent degeneration and this was slightly more marked in the cervical region than in either the dorsal or lumbar region. By the Weigert-Pal method sections taken at various levels in the cord show some degeneration in the posterior columns. In the upper cervical region the degeneration was more marked in the postero-external columns than in the postero-internal, but below this level the degeneration was evenly distributed. The degeneration as shown by this method, was not marked, but the columns are paler than the normal tracts.

By van Giesson's method the cells of the anterior horn appeared normal and there was no marked increase of the interstitial tissue in the posterior columns. Clarke's column appeared normal, but Lissauer's tract contained some degenerate fibres.

Nature of growth.—The growth is composed of cells of irregular shape lying in a matrix of fine fibrils. (Glioma.)

Case 11.—E. H., a coach-builder, aged 21 years, was admitted into the National Hospital under the care of Dr. Beevor on March 4, 1899. The family history was unimportant, and his health had been good until September, 1897, when headache, vomiting, diplopia, and failure of sight set in. Seven months later he had become completely blind. The headache and vomiting persisted, and in February, 1899, he became deaf in the left ear, and the left side of the face became paralysed, and he became very somnolent.

On admission he was somnolent, and his cerebration was slow. Speech normal. Taste and smell absent. Vision, no light perception. Complete post-neuritic atrophy of discs. Absolute nerve deafness in left ear. Divergent strabismus, the left eye looking down and out. Conjugate deviation to right was very feeble, and accompanied by slow long-range nystagmus. Marked paralysis of left face, both upper and lower. Electrical reactions of face normal. Head retraction. Muscles of neck rigid. Slight weakness, tremor and incoordination of left arm. Gait normal, occasionally he staggered to the left. Sensation normal. Knee-jerks not well marked. Wrist and elbow-jerks absent. Double extensor response in plantars. Trephining for the relief of the intra-cranial pressure was resorted to and the lateral ventricle aspirated. Death from respiratory failure on March 27, 1899.

Duration of symptoms eighteen months.

Description of tumour (plate x.).—A large trephine hole existed over the left lateral lobe of the cerebellum. The skull was thinned almost to paper thickness on the right side of the middle fossa. The right temporo-sphenoidal lobe was noticed to be very adherent to the dura mater at its apex, and after removal of the brain from the cranial cavity a large encapsulated tumour measuring 7 by 7 cm. was seen to occupy the right middle fossa. It compressed the right temporo-sphenoidal lobe, and lay almost loose in the cavity so formed. It was firm, hard in consistence, and intimately adherent to the dura, from which it appeared to grow. All the other organs in the body were healthy.

Microscopical examination (plate x.).—By the Marchi method there was marked degeneration in the posterior columns from the sacral to the cervical region. In the lumbar region the degeneration was most marked in the postero-external columns, very little being seen in the postero-internal column. In the cervical region, although the degeneration was most marked in the postero-external columns, yet there was also considerable change in the postero-internal column. The degeneration could be traced up to the funiculi gracilis and cuneatus. In the region of the olive there was some degeneration in the ascending root of the fifth of one side. In the pons there was practically no degeneration, although some black dots could be seen in the fillet. No change could be found in the pyramidal system, and no degeneration existed in the direct cerebellar tract. There were, however, some degenerate fibres in Lissauer's tract.

Posterior nerve-roots: In the cervical region one or two degenerate fibres could be seen, but the degeneration was very slight when compared to that in the cord, and in the dorsal and lumbar roots no degeneration could be found. By the Weigert-Pal method, apart from appearing paler than normal, the posterior columns showed no change.

No abnormality could be detected either in the cells of the anterior horn or of Clarke's column by Nissl's method.

Nature of growth.—The growth consisted of spindle-cells with large nuclei and alveolar spaces. (Spindle-celled sarcoma.)

Case 12.—E. B., a clerk, aged 34 years, was admitted into the National Hospital under the care of Sir William Gowers on February 3, 1899. Seven weeks before admission, when in good health, he was suddenly seized in the night with headache, vomiting, and delirium. Severe pain in the right side of the head and vomiting persisted, and he had four or five slight fainting attacks, followed by mental peculiarity lasting some minutes. Fourteen days before admission his sight began to fail. On admission his mental state was facile and grandiose, not unlike that often seen in "general paralysis." Intense double optic neuritis. Weakness of both external recti and of the left side of face (cerebral type). Slight weakness and some tremor of left arm. Left wrist and elbow-jerk absent. Knee-jerks present L. > R. Plantar reflexes, flexor responses. The skull was opened for the relief of optic neuritis.

Subsequently severe left hemiplegia came on gradually, and he died of respiratory failure on April 17.

Duration of symptoms four months.

Description of tumour (plate xi.).—An opening in the skull was present over the right cerebellar region. There was marked flattening of the convolutions. Some adhesions to the dura mater were present over the right temporo-sphenoidal lobe. On examining the base of the brain the right temporo-sphenoidal lobe was found to be implicated by a tumour which protruded through the cortex in the hinder portion of that lobe. The edges of the tumour were hard and raised, and presented an irregular surface. The cerebellum on the same side had lost a considerable amount of its substance along the posterior margin owing to the operation. No other abnormality was noticed in the cerebrum or medulla.

On making a horizontal section through the brain a large tumour was seen occupying nearly the whole of the middle third of the brain on the right side. The margins of the tumour were ill-defined, and consisted of several layers, a pale yellowish central portion, a green translucent portion, and outside this the white tumour substance merged into the brain substance proper. The corpus striatum, the lenticular nucleus, and the internal capsule were all pushed forward by the tumour. The tumour measured 6 by 6 cm.

Microscopical examination (plate xi.).—(The examination of the head only having been allowed.) At the lowest point of the cord obtainable, viz., about the level of the first cervical root, there was marked degeneration in the posterior columns, Burdach being more affected than Goll. There was also degeneration in the decussating fibres of the pyramid.

In the medulla there was the same marked degeneration in the posterior columns, and there was also a good deal of diffuse staining, too general to be described in detail.

At the level of the olive there was a good deal of degeneration in the restiform body, and the substantia gelatinosa, and some degeneration in one pyramidal tract.

At the level of the posterior corpora quadrigemina there was degeneration in the decussation of the superior cerebellar peduncle, and the fillet on the one side contained a few degenerate fibres, and on the other side numerous degenerate fibres.

By the Weigert-Pal method the cord appeared normal. There was, however, a small, very pale area situated in the peripheral portion of the antero-lateral tract (probably a normal condition).

Nature of growth.—The tumour appeared to be an irregular-celled sarcoma. The cells varied greatly in size, and were set loosely apart. (Irregular-celled sarcoma.)

Case 13.—G. H., a coachman, aged 64 years, was admitted into the National Hospital under the care of Sir W. Gowers on July 7, 1899. His previous health had been good. Five weeks before admission he was noticed to be mentally strange. This continued till a fortnight later, when, on getting into bed, he fell down and immediately vomited. The next morning he was noticed to have weakness of the right face. After this right hemiplegia and aphasia slowly came on. He gradually sank into a comatose condition, and died six weeks after the onset of symptoms. Headache had not been complained of. Condition on admission:—Double optic neuritis. Complete right hemiplegia and aphasia, semi-comatose. The right knee-jerk was just obtainable, the other deep reflexes were absent.

Duration of symptoms six weeks.

Description of tumour (plate xii.).—The convolutions were somewhat flattened. Situated in the left temporo-sphenoidal lobe was a spot over which the vessels were dilated and on palpation, although the surface felt soft the subjacent tissue was hard and nodular. A similar patch existed in the situation of the left angular gyrus. The right lateral sinus was absent from its origin to the torcular herophili. On making a horizontal section through the brain, two tumours were seen, the one occupying the posterior part of the first and second temporo-sphenoidal convolutions of the left side, and extending deep into the cerebral substance, the other occupying nearly the whole of the anterior part of the temporo-sphenoidal lobe. This growth was entirely separate from the other tumour, and had undergone some hyaline change. The lateral ventricles were not distended. The growth itself was hard and yellowish in colour, without distinct margins and obviously infiltrating the surrounding brain tissue. The one growth measured 5 by 3 cm. and the other 2 by 2 cm.

Microscopical examination (plate xii.).—By the Marchi method the lumbar and sacral region of the cord appeared perfectly normal. In the dorsal region there were a few degenerate fibres in the posterior columns, and in the upper cervical region there was a marked area of degeneration corresponding to about the fourth or fifth root on one side. This degeneration could be traced up to the funiculus cuneatus. The condition was present on both sides of the cord, but was far more marked on the one side than the other. There were also some degenerate fibres in the crossed pyramidal tract of the same side, as that on which the greater amount of degeneration existed in the posterior columns.

The degeneration was slight when compared to some of the other cases. The posterior root ganglion examined was normal.

By the Weigert-Pal method the cord appeared perfectly normal. Lissauer's tract was normal.

By the Nissl method, although the cells in the anterior horn appear less numerous than normal, it could not be said that there was any pathological change. There were numerous corpora amylacea in the white matter of the spinal cord in all regions, but they were more numerous in the cervical than in other regions. These bodies were not visible by the Marchi or Weigert-Pal methods. Clarke's column was natural.

Nature of growth.—The growth was very irregular, hæmorrhage having occurred into it at various points, and at others it had undergone gelatinous degeneration. It was formed of a loose network with scattered nuclei. (Glioma.)

Case 14.—E. E., aged 50, was admitted to the National Hospital under the care of Dr. Beevor, on July 31, 1899.

One month before admission, her husband, on returning home one night, found her sitting in a chair, unable to move the right arm or leg, nothing was noticed in the face. She could speak correctly, but gradually lost sensible speech. She had had two or three attacks of vomiting since the onset of the illness, but had not complained of headache. She knew people about her and could indicate her wishes.

On admission, the patient could sit up in bed and could talk but not sensibly, about a week later she rather rapidly fell into a comatosed condition. The pupils were small, the right being somewhat larger than the left, and neither reacted to light. There was slight squint due to weakness of the left internal rectus. There was slight neuritis in the right eye. Sensation was impaired all down the right side of the body and the corneal and conjunctival sensation was also diminished on the right side. The right arm and leg were absolutely flaccid. Reflexes: The arm-jerk on the right side was not obtained, but was present on the left. The right knee-jerk was not obtained, but the left was present. There was no ankle clonus. The plantar reflex on the right side gave an extensor response, and on the left stimulation on the inner side of the sole gave a flexor response while on the outer side an extensor response was obtained.

The patient gradually became more comatosed and died, and on the last day of life neither the knee-jerks nor the plantar reflexes were obtainable.

Description of tumour (plate xiii.).—There was flattening of the convolutions, especially in the region of the marginal and angular gyrus of the left side. On the right side there was no flattening or the convolutions which on the other hand appeared rather shrunken, and there was considerable compensatory œdema. On examining the base of the brain it was seen that the left crus was of a grey colour, and very considerably wider than the right. A section was made in a horizontal direction through the brain and a large tumour was seen to occupy the left hemisphere measuring 5·5 by 8 cm. The growth was situated in the posterior portion of the hemisphere, and extended forward to the hinder part of the left lenticular nucleus, and involved the left optic thalamus. The growth did not extend into the left lateral ventricle, but by its size had narrowed the limits of the ventricle. At no point did the growth reach the surface of the hemisphere. The growth appeared like a fleshy mass which had undergone yellow softening at its centre. The point of origin of the growth appeared to be about the optic thalamus. In a downward direction the growth extended into the left crus and tegmentum, but did not involve the corpora quadrigemina.

Microscopical Examination.—Marchi. No degeneration was found in the spinal cord either in the posterior or lateral columns. At the level of the olive only a very few degenerate fibres could be seen in the left pyramid and even in the pons where the growth actually invaded the left pyramid, degeneration could only be seen in the immediate neighbourhood of the tumour.

By the Weigert-Pal method no change could be detected in the spinal cord or the medulla; in the pons, however, there was a large area of unstained tissue situated on the left side, and which involved nearly the whole of the left pyramid, fillet, and superior cerebellar peduncle.

By the Nissl-method no change could be detected in the cells of the anterior horn.

Nature of growth.—The growth was composed of elongated nuclei arranged in a somewhat irregular manner in bundles which ran in various planes. There was very little alveolar structure, the growth being uniform throughout, and it was moderately vascular. (Spindle-celled sarcoma.)

Case 15.—W. W., aged 50, was admitted into the National Hospital, under the care of Dr. Tooth, on August 23, 1899.

Twelve months before admission he fell from a wall and struck the left side of his head, and ever since a week or two after this he had complained of headache at the back of his head. Six weeks after the accident he had a fit, in which he lost consciousness, fell, bit his tongue, and was convulsed all over. After this the fits recurred every fortnight. There was no warning at first, but his wife says that now he knows when a fit is coming on, and he has time to lie down.

During the fourteen days preceding admission the patient had vomited, but previous to this the patient had had no vomiting. His eyesight had been failing, and he had been "strange in his head"

On admission he was in a confused mental condition, but could answer questions, and used correct language. There was double optic neuritis with hæmorrhages. Both pupils reacted readily to light. There was slight right facial weakness, with distinct ptosis of the right eye-lid. Both arms and legs moved normally, but the limbs were flaccid.

Reflexes: Elbow and wrist-jerks were equal. The knee-jerk was present on the right side, and very difficult to obtain on the left. The plantar on the right side gave a flexor response while on the left it was sometimes absent, sometimes gave an extensor response. There was tenderness on pressure on the left side of the cranium above and also behind the ear.

The patient gradually became comatose, and died three days after admission.

Description of tumour (plate xiv.).—There was slight flattening of the convolutions and very marked bulging in the left temporo-sphenoidal region. The convolutions were broader than normal, and there was obviously a tumour infiltrating the left temporo-sphenoidal lobe; on section the growth was seen to occupy the posterior and lower portion of the left temporo-sphenoidal lobe. The tumour had undergone cystic degeneration and the cyst was filled with green gelatinous material. The growth had no definite margins. The basal ganglia and the internal capsule appeared healthy and not affected by the growth. The growth measured 5 by 6 cm.

Microscopical examination.—Marchi's method (plate xiv.). The sacral, lumbar and dorsal cord appeared normal, and at the level of the fifth cervical there were two obviously degenerate roots; the one on the left side originated probably from the seventh cervical root, and the one on the right side from the sixth root.

The degenerated root on the left side was the more affected. This degeneration could be traced up into the funiculus cuneatus. No degeneration was present above the posterior column nuclei.

By the Weigert-Pal method the cord appeared perfectly normal, and by the Nissl method the cells of the anterior horn appeared normal.

Posterior root ganglion: The cells appeared perfectly normal, although there was considerable pigmentation.

Nature of growth.—The growth was composed of fibrous tissue with elongated nuclei, having an alveolar arrangement, the alveoli being filled up with nuclei of somewhat irregular size. In other portions of the tumour the alveolar arrangement was less marked. There was very little evidence of degeneration in the tumour, and at its margins where it infiltrated the brain it was extremely vascular. (Mixed-celled sarcoma.)

Case 16.—W. G. S., aged 7 years, was admitted into the National Hospital under the care of Dr. Tooth on January 6, 1899, complaining of vomiting and "tumbling about." There was a history of phthisis in the family.

The patient was quite well up till the age of 2 years, when it was noticed that he began to tumble about and to be clumsy with his hands. This had gradually increased till the time of admission. Since six months before admission he had vomited occasionally. No headache or fits had been noticed. On admission he was a particularly intelligent, healthy-looking child. Smell, taste and hearing acute. Vision $\frac{6}{24}$ and J 4 with each eye. Marked post-neuritic atrophy of both discs.

Marked spontaneous nystagmus, quick movement to right. Wide range nystagmus on deviation, more marked on deviation to right. Slight weakness of upper right face. Marked weakness of lower right face. Electrical reactions of face normal. Distinct bulging of skull over the left cerebellar region tender to pressure. Intense jerky incoordination of all the limbs much more marked on the left side. Left limbs slightly less powerful than right. Reeling gait. He always fell straight backwards when standing up. Knee, wrist and elbow-jerks brisk and equal. Plantar reflexes were flexor responses.

The left side of the cerebellum was exposed by Mr. Horsley on February 2, 1899, and a cyst containing about an ounce of clear fluid evacuated, which appeared at one spot on the surface of the left lateral lobe of the cerebellum. As there was no obvious sign of growth in the cyst wall, after the evacuation of the cyst the wound was at once closed.

Three days after the operation the knee-jerks were absent. On the fourth day the right knee-jerk was obtained, but after this the knee-jerks were persistently absent. No other change in the physical signs took place. He died suddenly and unexpectedly eleven days after the operation.

Duration of symptoms three and a half years.

Description of growth (plate xv.).—There was an opening in the skull over the left lateral lobe of the cerebellum. The convolutions were not flattened, and the surface of the cerebrum appeared normal. The left lateral lobe of the cerebellum was adherent to the incision in the dura mater, but was easily separated from it, and on inspection presented very little abnormal. A hard tumour could, however, be felt, occupying the middle lobe and extending laterally more to the left than to the right. On section the tumour was found to involve the left corpus dentatum. It grew ventrally into the upper and left side of the pons, and extended upwards to a point just below the corpora quadrigemina. In a downward direction the growth seemed to involve the left middle and inferior cerebellar peduncle and the dorsal portion of the medulla on the left side.

Microscopical examination.— The cord appeared perfectly normal to all methods of examination; no degeneration could be shown by the Marchi method, even in the immediate neighbourhood of the tumour, though its limits are distinctly shown by the Weigert-Pal method.

Nature of growth.—The growth appeared to be formed of irregular-shaped cells; in some parts the cells were widely separated. There were numerous corpora amylacea in portions of the tumour. (Glioma.)

Case 17.—M. P., aged 47, was admitted to the National Hospital, under the care of Dr. Ferrier, on October 12, 1898.

For three to four years the patient had had a rushing noise in the right ear. Eighteen months ago she found that she was deaf in the right ear. She had suffered from vertical and occipital headache for three years.

One year ago she had an attack in which the legs "went stiff" while walking; there was no loss of consciousness, and no twitching, and the stiffness was only momentary. Ever since this time she had been subject to occasional attacks of rigidity in all four limbs; she felt giddy, but did not fall down.

Three weeks ago her eyesight began to fail, and during the week before admission it had rapidly deteriorated. She had occasional attacks of complete blindness. She had had severe vertical headache for three years, occasionally spreading down the back of the neck. She had been very sick for a fortnight.

On admission she was a poorly nourished woman. Smell and taste were normal. She was totally deaf in the right ear. There was intense double optic neuritis. There was no weakness or ataxy of the trunk or limbs, and the gait was normal. The knee-jerks were normal and equal. There was no ankle clonus.

On November 30 Mr. Horsley removed the calvarium from the right occipital region, and on December 6 he opened the cerebellum, but was unable to find the tumour. The patient died on December 15.

Description of tumour (plate xvi.).—There was an opening in the right posterior fossa, due to the operation. The convolutions did not appear flattened. The base of the right lateral lobe of the cerebellum was broken up, as the result of the operation; projecting from the under-surface of the anterior part of this lobe of the cerebellum was a tumour measuring 3 by 5 cm., growing from the flocculus and pressing on the right side of the pons, so as to make it quite flat. The fifth nerve on this side was seen lying against the tumour, and was quite flat and tape-like.

Microscopical examination (plate xvi.).—By the Marchi method, there was marked degeneration in the funiculi gracilis and cuneatus, being more in the latter than the former. In the cervical region of the cord, the degeneration of the posterior columns was well marked, and affected the column of Burdach more than the column of Goll. Below the cervical region, the degeneration was much less marked, and was more scattered, but was present as low as the sacral region to a slight degree. There was no degeneration of any other tract in the cord. By the Weigert-Pal method, the cord appeared perfectly normal.

Nature of growth.—The growth was composed of elongated cells of uniform size and character, arranged in various planes. (Fibro-sarcoma.)

Case 18.—J. F., aged 5, was admitted to the National Hospital, under the care of Dr. Ferrier, on June 10, 1898.

Fourteen months before admission he had had whooping cough and broncho-pneumonia, and was in bed for ten weeks. Whilst in bed he had severe pain in the right side of the head, and his right arm was noticed to be weak. From this illness he recovered completely.

Five months before admission he had measles, and a month later he began to complain of headache. Six weeks before admission he was noticed to stagger, and complained of giddiness, but had neither headache nor vomiting.

On admission he was a well-nourished, intelligent boy. Double optic neuritis was present, but there was no weakness of the limbs nor ataxy while in bed. His gait was reeling and unsteady, and he tended to stamp the heels on the ground. He tended to fall when the eyes were shut. Reflexes: the knee-jerks were present and equal; there was no ankle clonus; the arm-jerks were equal. There was some prominence over the left side in the cerebellar region. On June 28, Mr. Horsley enucleated a tumour from the left lateral lobe of the cerebellum. The child developed symptoms of tubercular meningitis, wasted rapidly, and died on September 16.

Description of tumour.—There was a large opening in the left occipital region. The convolutions were flattened, and there was obvious tuberculous meningitis at the base. The left lateral lobe of the cerebellum was broken up and softened, and was adherent to the dura mater. The ventricles were much dilated. The spinal cord showed a marked degree of tuberculous meningitis, and this extended down to the lumbo-sacral region.

Microscopical examination of cervical region of the cord showed no degeneration either by the Marchi or Weigert-Pal methods.

Nature of growth.—Tuberculous.

Case 19.—L. S., aged 5 years, was admitted into the National Hospital, under the care of Sir William Gowers, on March 17, 1899, complaining of headache, loss of sight, and inability to stand or sit up. Seven months before admission, headache, vomiting, and inability to walk (staggering) had come on, and it was noticed that the head was constantly inclined to the right shoulder. Two months before admission she became unable to sit up, and she became gradually deaf in the left ear. For a month head retraction had been noticed.

On admission she was semi-comatose. Head retraction.

Hydrocephalic cry. Severe optic neuritis. Complete deafness of left ear. Pupils dilated. Nystagmus. General paresis and general coarse tremor on movement.

Knee-jerks present and equal. Plantar reflexes were extensor responses. On April 7, she developed measles, and the knee-jerks were noticed to be absent. She died on April 9, without further manifestation of symptoms.

Duration eight months.

Description of growth (plate xvii.).—The left lateral lobe of the cerebellum was enormously distended by a large cyst which appeared on the dorsal surface and compressed the right lobe across the middle line, the right lobe of the cerebellum appeared to be normal. After hardening in formalin a section through the cerebral hemispheres showed them to be perfectly normal and there was no distention of the ventricles. On section through the cerebellum the cyst was found to occupy almost the whole of the left lobe, only a thin layer of cerebellar substance covering the tumour. The cyst was filled with a green clear jelly-like substance, and measured 7 by 4 cm. in the antero-posterior and the lateral diameters respectively. The wall of the cyst measured about 2 mm. and was composed of two layers, the inner of which could be easily shelled out over its greater extent but was adherent and merged into the growth on the inner side of the lobe.

Microscopical examination (plate xvii.).—By the Marchi method there was marked degeneration of the posterior columns from the sacral to the cervical region, but the degeneration was more marked in the column of Burdach and the funiculus cuneatus than in the column of Goll and the funiculus gracilis. No degeneration could be seen above the posterior column nuclei. The posterior roots showed marked degeneration in the cervical region, less in the dorsal, and again more marked change in the lumbar region. By Weigert-Pal and Nissl methods the cord appeared normal. Clarke's column was normal and Lissauer's tract was unaffected.

Nature of growth.—The tumour showed characters that it was difficult to distinguish from brain tissue undergoing softening but it appeared to be a glioma with the cells ar apart. The cystic part of the tumour was found to consist of a meshwork of the finest fibres. (Glioma.)

Case 20.—W. G., aged 6 years, was admitted into the National Hospital under Dr. Tooth, on February 3, 1899, complaining of headache, sickness, and staggering. The family history was unimportant and his health had been good previous to this illness. Three months before admission, headache and vomiting set in suddenly and persisted, and on several occasions he had attacks of trembling all over in his sleep. Six weeks later he began to walk badly and to tumble about.

On admission he was a healthy-looking child. He complained constantly of headache over the right eye. When sitting up the posture of the head was constantly as follows: right ear inclined to right shoulder, face turned to left, head bent forwards. Mental state intelligent. Special senses normal. Optic discs showed intense recent neuritis.

Marked nystagmus more intense on looking to right. Slight right lower facial weakness. Intense ataxy of left limbs, slight ataxy of right limbs. He walked unsteadily and reeled a great deal. When standing feet together he always fell straight backwards. Wrist and elbow-jerks present, knee-jerks sometimes brisk, sometimes difficult to elicit, even with reinforcement.

Mr. Horsley removed the calvarium and opened the dura mater over the left lateral lobe of the cerebellum. Some hours after the operation the patient became much worse, and the site of the operation was found to be bulging. On re-opening the flap a large tumour which had ruptured the left lobe of the cerebellum and escaped, was found lying free in the wound.

Description of tumour (plate xviii.).—There was marked flattening of the convolutions and dilatation of the ventricles. The left lateral lobe of the cerebellum was almost completely destroyed, being converted into a thin walled cavity from which a tumour measuring 7 cm. by 3·5 cm. had escaped. The cavity in the left lateral lobe was in direct communication with the fourth ventricle and extended upwards compressing the medulla and pons and dilating the iter as far as the posterior corpora quadrigemina. At a section made between the medulla and pons the cavity measured 3 cm. by 1·5 cm., and above this point it gradually narrowed down. The pons is so compressed that at its junction with the medulla it measured only 8 mm. in diameter. The tumour which had occupied the above cavity was dark in colour, friable, and evidently contained much blood.

Microscopical examination (plate xviii.).—By the Marchi method the cord in the cervical region showed degeneration in the posterior columns and in the direct cerebellar tract of both sides. Further examination was impossible as the removal of the spinal cord was not allowed.

Nature of growth.—The growth was an extremely vascular small round-celled sarcoma.

Case 21.—M. B., a woman, aged 30 years, was admitted into the National Hospital, under the care of Sir W. Gowers, on April 24, 1899. Three years before admission, occipital and right frontal headache set in; this was followed by giddiness, staggering, and diplopia, and a year before admission she became slowly blind, and also completely deaf in the left ear.

On admission there was no mental defect. Consecutive optic atrophy. Complete nerve deafness in left ear. Nystagmus most marked on deviation to left. Slight weakness of the whole left face. When standing the head always assumed the following position: the left ear was inclined to the left shoulder, and the face was turned slightly to the right. There was distinct bulging of the calvarium over the region of the left lateral cerebellar lobe. She fell to the left when standing. There was marked incoordination in the left limbs. She complained of severe pains in the legs, as if she had been walking too far. There was marked hypotonia of the muscles of the legs and a slighter hypotonia of the arm muscles. The knee-jerks were present and equal. Plantar reflexes were flexor responses.

The tumour was removed in part from the left lateral lobe of the cerebellum on June 20.

She died on July 20.

Duration of symptoms three years and three months.

Description of tumour (plate xix.).—There was an opening through the skull in the left occipital region. The surface and convolutions of the brain appeared normal; nothing abnormal was noted on the base of the cerebrum; the left posterior fossa was found to be occupied by a firm and hard tumour, adherent to the petrous bone, but not growing from it; the whole of the left lateral lobe was occupied by this tumour, and it pressed upon the left side of the pons, displacing it to the right and making a depression on its surface. An incision was made right through the cerebellum, and the tumour was seen to be infiltrated with blood, probably as the result of the operation. The tumour, on section, was hard and firm, and evidently very fibrous, although at places of a pale yellow colour, suggesting that it had undergone caseation. The lateral ventricles, as well as the third and fourth and iter, were greatly dilated.

Microscopical examination.—By the Marchi method, no degeneration could be seen, either in the posterior or other columns of the cord. In the dorsal portion of the medulla there was some degeneration in the restiform bodies and reticular formation, but this does not pass down the cord. The posterior root ganglion appears normal, the cells being somewhat pigmented. By the Weigert-Pal and Nissl methods the cord appeared normal. Lissauer's tract and Clarke's column were also natural.

Nature of growth.—The growth appeared composed of elongated cells, arranged in bundles and running in different planes. The nuclei were very irregular in size, some being large and elongated and others small and round; the tumour was not unlike a fibroid tumour of the uterus. (A fibro-sarcoma.)

Case 22.—H. C., aged 7 years, was admitted into the National Hospital, under the care of Dr. Hughlings Jackson, on March 13, 1899. There was a family history of phthisis. His illness began a month before admission, with occipital headache and vomiting. A fortnight later he began to stagger in his walking.

On admission he was mentally very stupid, and presented the following signs:—Double optic neuritis. Nystagmus chiefly to right. Slight right facial weakness. Inco-ordination in all four limbs much more marked on right side. Gait staggering, leaning forward, and lurching to either side. No weakness or sensory change. Knee, wrist, and elbow-jerks R. > L., and subnormal; sometimes absent. Plantars flexor responses. He died on June 1, 1899.

Duration of symptoms four months.

Description of tumour (plate xx.).—The convolutions were flattened, but otherwise normal, and the surface of the cerebellum appeared natural. On section, however, a large tumour was seen situated exactly in the middle line, being composed of soft pulpy substance, limited by a sharp line from the cerebellar substance. The growth protruded into the fourth ventricle, and blocked it up. The growth measured 5 cm. in diameter, and was spherical in shape. Both lateral ventricles were considerably dilated.

Microscopical examination (plate xx.).—By the Marchi method, there was no degeneration in the sacral region of the cord; a little scattered degeneration was present in the posterior columns in the lumbar region, becoming more marked in the dorsal region and in the cervical, being fairly well marked in the postero-external columns, and slight in the postero-internal columns. There were a few scattered degenerate fibres in the pyramidal tracts of both sides. Lissauer's tract appeared normal. The cord appeared perfectly normal by the Weigert-Pal method, and the cells of the anterior horn also appeared normal by the Nissl method.

Nature of growth.—The tumour was composed of large nuclei, lying in what appears to be a nearly homogenous matrix;

in some parts of the tumour these nuclei were so densely packed together that hardly any matrix existed, while in other parts they were widely separated. The nuclei were very large and irregular both in size and shape. In other parts of the growth, the arrangement was more alveolar, with bands of fine fibrous tissue forming the alveoli. (Alveolar sarcoma.)

Case 23.—W. R., aged 30, a gardener, was admitted into the National Hospital, under the care of Sir William Gowers, on September 12, 1898. His illness began in January, 1898, with headache and vomiting. Since February, 1898, he had a constant feeling of unsteadiness when on his legs. In August, 1898, his sight began to fail rapidly and he staggered and fell repeatedly when walking.

On admission he was mentally very dull. There was intense optic neuritis going on to atrophy. He could just count fingers at six inches. No deafness. Marked nystagmus. Marked weakness of left face (upper and lower). Electrical reactions of face normal. Slight weakness of right arm and leg. He leant and fell to the right constantly when standing, and lunged to the right when walking. Sensations normal. Wrist, elbow, and knee-jerks subnormal. R. > L. Plantar reflexes were flexor responses.

During the next three months he became quite blind. Marked ataxy of the right limbs developed. The left facial palsy became more marked, no electrical alteration accompanying the weakness. The right hemiparesis of limbs became more marked. The deep reflexes remained. R. > L. and subnormal. The right knee-jerk was sometimes absent. Head retraction was noticed on several occasions. The plantar reflexes were always flexor responses.

He died on July 19, 1899.

Duration of symptoms nineteen months.

Description of tumour (plate xxi.).—On the under and external surface of the cerebellum is seen a dark, rounded tumour, hardly raised above the surface, with several large vessels running over its surface; on making a section through the cerebellum, a cyst, measuring 3·5 by 4 cm., is seen occupying the whole of the central portion of the right lateral lobe. The cyst is thin and easily separated from the surrounding brain substance, except at its outer side, where it forms part of the growth. There are several other smaller cysts filled with gelatinous material. In the left cerebellar lobe another growth could be seen occupying the central portion of the lobe; it was hard and firm, and had no distinct margin separating it from the normal brain tissue that surrounds it.

Microscopical examination (plate xxi.).—By the Marchi method there was slight degeneration in the posterior columns in the sacral and lumbar regions, and in the dorsal it was still slight. It increased somewhat in the lower cervical region, where it was almost limited to the postero-external columns, and it was traceable to the funiculus cuneatus, the funiculus gracilis escaping altogether. By the Weigert-Pal method the cord appeared perfectly normal; the tract of Lissauer was also normal. By the Nissl method the cells of the anterior horn and of Clarke's column appeared normal.

Nature of growth.—The tumour was extremely vascular; there being large blood spaces surrounded by irregularly-formed fibrous tissue; in other spaces, where there was no blood, a fine meshwork existed, with scattered cells of a gliomatous appearance. In another portion of the tumour it appeared like cartilage, but the cell spaces were very irregularly formed. (Glio-sarcoma).

Case 24.—E., aged 6, was admitted to University College Hospital, under the care of Dr. Risien Russell, on September 21, 1898, with the history that, except for measles two to three years ago, she had been perfectly well till six to seven months before admission, when she had an attack of vomiting. A second attack occurred about three weeks later, with headache, and the attacks recurred at intervals of about a week ever since. She has been losing flesh rapidly of late. The sight has been failing for the last three to four days.

On admission the child was well nourished, the head was large, and the child was intelligent. The eyesight was defective, and optic neuritis was present in both eyes. There was no nystagmus, no facial weakness, and the hearing was equal on the two sides. No loss of power in the limbs could be found, but there was slight ataxy of the right arm. The gait was unsteady, and there was slight incoordination in the movements of the right leg. The head was in the right cerebellar attitude, *i.e.*, right ear inclined to right shoulder and face turned to left. The knee-jerks could not be obtained, and the wrist and triceps-jerks were also absent. The child died in October.

Description of tumour (plate xxii.).—The convolutions were flattened, and the lateral ventricles dilated. A large tumour was found to occupy the left lateral lobe of the cerebellum, and extended across the middle line. The tumour was of uniform consistence, with a fairly sharply-defined margin.

Microscopical examination of the cord (plate xxii.).—By the Marchi method there was some scattered degeneration in the lumbar region of the cord, limited to the postero-external columns. In the dorsal region the degenerated fibres seemed to have accumulated in the ventral portion of the posterior internal column. In the lower cervical region there is again more marked degeneration in the postero-external columns, and this can be traced up through the cervical region into the funiculus cuneatus. There were a few degenerate fibres in the funiculus gracilis. All the other regions of the cord appeared perfectly normal. By the Weigert-Pal method the lumbar and dorsal regions appeared perfectly normal. In the cervical region a small area, lying between the postero-internal and external columns, was paler than the other portions of the posterior columns, and seemed to contain fewer fibres. This pale area was symmetrical on the two sides.

Nature of growth.—The tumour was composed of cells lying in a meshwork of fine connective tissue; the growth appeared quite uniform in structure, and had undergone very little degenerative change. (Glioma.)

Case 25.—M. C., a nursemaid, aged 24 years, was admitted into the National Hospital, under Dr. Colman, on September 2, 1898, complaining of headache, sickness, and dimness of vision. Her father died of consumption, otherwise her family history was unimportant. She had always been strong and healthy till nine months before admission. Her sister stated that for five years she had been subject to neuralgic pain in the left temple, and that during this time she had attacks of dimness of vision, lasting a few minutes at a time. During the year preceding admission these attacks had been much more frequent. In January, 1898, she noticed dimness of vision at night. A month later severe headache and vomiting occurred and persisted. The headache, vomiting, and dimness of sight became steadily worse until a fortnight before admission, when the headache ceased. She had noticed some unsteadiness in standing for three months.

On admission she was a healthy-looking girl of good intelligence. She was evidently very ill, and was constantly vomiting. There was intense double optic neuritis, and vision was reduced to form-perception. Marked spontaneous nystagmus. She walked unsteadily, but on account of her general physical condition and the vomiting that the least movement brought on, no importance could be attached to this symptom. There was very marked muscular hypertonia of the limbs. The knee, wrist, and elbow-jerks were absent, and were never obtained; otherwise, the special senses, cranial nerves, motion, sensation, and the sphincters were normal.

On September 17 she became delirious, and died suddenly six hours later. No fresh symptom had developed.

Duration of symptoms eight months.

Description of tumour (plate xxiii.).—The convolutions were not flattened, and the brain, as a whole, appeared normal in size and consistence. After hardening, a horizontal section was made through the two cerebral hemispheres, and an exceedingly vascular tumour was seen to occupy the posterior horn of the left lateral ventricle growing apparently from the choroid plexus. There was obvious hæmorrhage into the tumour, so that in colour it resembled hæmorrhage rather than growth. Its greatest length was in the antero-posterior diameter, being 5 cm., while its greatest width was about 3 cm. There was some blood-clot in the anterior horn of the left ventricle.

Microscopical examination (plate xxiii.).—By the Marchi method there was some degeneration in the posterior column of the cord, most marked in the mid-dorsal region, where the degenerate roots can be seen entering the cord, and this degeneration was traceable up the cord, becoming more diffuse in the cervical region. The degeneration was only of moderate degree, and at no level could be said to be marked. There were a few degenerate fibres in the lumbar and sacral region of the cord. By the Weigert-Pal method the cord appeared perfectly normal.

Nature of growth.—The growth was extremely vascular, composed of cells of irregular size and shape, lying widely separated in a matrix which stained badly, and in which degeneration had taken place. There were numerous masses of brown pigment, probably altered blood clot. (Glio-sarcoma.)

Case 26.—D. C., a clerk, aged 27 years, was admitted into the National Hospital, under the care of Dr. Bastian, on February 14, 1898. In February, 1897, he constantly fell asleep over his work, and from this time left hemiplegia slowly developed. In September, 1897, he had headache for the first time, and his sight began to fail. Up to the time of his admission he had had no fits and no vomiting.

On admission his mental state was intelligent. He frequently dropped off to sleep at his meals. Double optic neuritis. Rigid left hemiplegia. No hemianopia. No hemianæsthesia. Knee, wrist and elbow-jerks L. > R. Left foot clonus.

On May 10 he was semi-comatose, and vomited frequently. Left hemianæsthesia was present. He was absolutely blind.

On August 22 left-sided fits, without loss of consciousness, occurred and recurred at intervals for some months. The left hemiplegia became absolute.

In October right hemiplegia slowly came on, and after this right-sided convulsions, without loss of consciousness, occurred. Double foot clonus and double extensor response developed. Death occurred on February 8, 1899, from respiratory failure.

Duration of symptoms two years.

Description of tumour (plate xxiv.).—There was marked flattening of the convolutions on both sides, with bulging on the right side. On section through the brain, a tumour, measuring 4·5 cm. by 4·5 cm., was seen to occupy the right optic thalamus, and extended down into the right crus. The tumour was of yellowish colour, and built up of concentric laminæ; it was extremely hard, and showed no tendency to soften. The lateral ventricles were dilated. There was an old focus of tubercle at the apex of the left lung.

Microscopical examination (plate xxiv.).—By the Marchi method degeneration in the pyramidal tract of the right hemisphere could could be traced through the pons into the medulla and down to the sacral region of the cord. Sections through the middle of the pons showed degeneration in the cerebellar peduncle of the same side, and also, to a lesser extent, in the fillet. At the level of the olive there were some scattered black dots in the raphe, and definite degeneration in the fibres of the twelfth nerve. The fillet degeneration could be traced down across the raphe into the nuclei gracilis and cuneatus of both sides, the opposite one being, however, most affected. There was some degeneration in the direct cerebellar tract on both sides. Below the decussation of the pyramids there was very little degeneration in the posterior columns, and that was limited to the cervical region. Some degeneration could be seen in the posterior longitudinal bundle of the same side as the lesion. By the Weigert-Pal method there was marked degeneration of the pyramid, both direct and crossed, but the posterior columns were natural. There was marked degeneration in the fillet of the same side, but both posterior longitudinal bundles and superior cerebellar peduncles appeared normal. By the blue-black method the cells of the anterior horn and of Clarke's column appeared normal. The right and left median and anterior crural nerves were examined, and the left median showed most extensive change, not only by the Marchi but also by the Weigert-Pal method; the other nerves appeared normal.

Nature of growth.—On section, the growth showed a degenerate centre surrounded by a large number of small round cells, among which are many well-formed giant-cells; so marked was this appearance that the tuberculous origin of the tumour could not be doubted; no tubercle bacilli could, however, be found (Tuberculous tumour.)

Case 27.—H. F., aged 18 months, was admitted into the National Hospital, under the care of Dr. Buzzard, on May 9, 1899. Eight weeks before admission, strabismus and head retraction were noticed. A few days later the sight was noticed to fail. At the end of a fortnight paralysis "all over" came on, and the child lost its speech. On admission he was semi-comatose, with convergent strabismus and complete ophthalmoplegia in right eye. Nystagmus in left eye. Neither pupil reacted to light. Optic discs normal. General paresis more marked on the left side. Head retraction. Slight hydrocephalus. The knee-jerks were absent, but on striking the left patella tendon, an adductor-jerk was obtained on the opposite side. He died on May 19.

Duration of symptoms nine weeks.

Description of tumour (plate xxv.).—There was marked flattening of the convolutions, otherwise the brain appeared normal. After hardening in formalin, the brain was cut in horizontal section. Both ventricles were enormously distended. A tumour was seen occupying the right optic thalamus; it extended into and involved the corpora quadrigemina, and passed over to the optic thalamus of the opposite side. It extended downwards to the commencement of the pons, and ventrally to the substantia nigra, but did not involve the crura. The growth was an infiltrating one, without definite margins, and towards the centre had a yellow granular appearance, but was hard and not caseous. Hæmorrhage had taken place into the tumour.

Microscopical examination (plate xxv.).—By the Marchi method there was very marked degeneration in the sacral region of the cord, leaving the septo-marginal tract almost unaffected, the degenerate fibres could be traced into the base of the posterior horns, and some also into the anterior horns. In the upper lumbar region the degeneration was fairly evenly distributed, but left the dorsal and median portion of the cord less affected; in the mid-dorsal region the column of Goll was more affected than that of Burdach. In the lower cervical region the entering roots were markedly degenerate, and the column of Burdach was markedly affected. The degeneration could be traced up to the nuclei gracilis and cuneatus. The direct cerebellar tract was unaffected, and the tract of Lissauer also escaped. In the medulla there was some degeneration in the fillet and in the remaining portions of the funiculi gracilis and cuneatus. In the pons the degeneration was again more extensive, and involved the posterior longitudinal bundle, the fillet, and the superior cerebellar peduncles on both sides. The posterior root ganglia, so far as the cells were concerned, appeared normal both to the Marchi and Nissl methods. Posterior nerve-roots appeared perfectly normal; no degeneration could be seen in them. By the Weigert-Pal method the cord, medulla, and pons appeared perfectly normal; Lissauer's tract was normal. By the Nissl method the cells, both of the anterior horn and of Clarke's column, appeared natural.

Nature of growth.—The growth was very vascular at its margins, and was formed, for the most part, of large round cells of uniform size, with distinct nuclei, there being comparatively little fibrous tissue; but at certain points, generally in the neighbourhood of vessels, there was extensive infiltration, with small round cells (sarcoma).

Case 28.—A. A., aged 7, was admitted into the Hospital for Sick Children, under the care of Dr. Lees, with the following history;—She had been quite well till eleven days previously; she then complained of pain in the back of her head, held her neck stiffly, and vomited frequently.

On admission she was drowsy, but would answer questions; there was slight facial weakness on the left side; loss of sensation of the left cornea and conjunctiva, and paralysis of the left external rectus. There was double optic neuritis. The knee-jerks were present. The child died the day after admission.

Description of tumour (plate xxvi.).—The convolutions were flattened, and there was considerable dilatation of both the lateral ventricles as well as the third and fourth. The pons appeared very much enlarged, and the left side larger than the right. On section, a firm, white, infiltrating growth was found to occupy the left side and extended across the mid-line into the right side. The other organs of the body were normal.

Microscopical examination.—No degeneration could be detected in the spinal cord either by the Marchi or the Weigert-Pal methods, and the cells appeared normal by the Nissl method. Section of the pons stained by the Weigert-Pal method show a large infiltrating tumour separating the fibres of the pons, but apparently not destroying them.

Nature of tumour.—The growth was composed of a meshwork of fine fibres, among which were scattered irregularly nuclei of uniform size, mostly angular in shape, and from some it would seem that fine prolongations can be traced into the meshwork. The growth is quite uniform in structure. (Glioma.)

Case 29.—E. J., aged 42, was admitted into the National Hospital, under the care of Dr. Beevor, on August 24, 1899.

Fourteen days before admission the patient began to have giddiness and severe neuralgic headaches, but previously to the onset of these she had been in particularly good health. The pain was referred to the frontal region of the skull. The headache increased, and twelve days after the onset she was found by her daughter in a dazed condition, complaining of intense pain in the head. She had an attack of vomiting. About 5 o'clock on the same day she was found lying on the bed in a semi-comatose condition. The dejecta were passed under her involuntarily; the coma deepened, and she was admitted into the hospital two days later.

On admission the patient was well nourished, and lay in bed with the legs drawn up, the arms flexed, and the head turned into the pillow, and all attempts to alter this position were resented. Respiration tended to assume the Cheyne-Stokes character; the right pupil was larger than the left, and did not react to light (previously dilated with atropine). The discs were hyperæmic, the edges blurred and streaky, and the veins swollen. No loss of power could be detected; the lower limbs tended to assume the flexed position, but were not rigid. Reflexes: the arm-jerks were present; the knee-jerks were present, but were not brisk; there was no ankle clonus, and the plantars gave a flexor response. No abdominal reflex was obtained. Urine 1024, no albumen or sugar.

Death occurred at 3 a.m. on the following day, respiration ceasing suddenly, followed after an interval of some minutes by heart failure.

Description of tumour (plate xxvii.).—There was marked flattening of the convolutions, but no tumour could be detected on the surface. On making an incision through the callosum, a cyst was seen lying below the anterior portion of the fornix, filling up the lateral communications of the lateral ventricles, and pressing down into the third ventricle, blocking up the foramen of Munroe. The cyst was somewhat pear-shaped. It was adherent to both choroid plexuses, and probably grew from the left. There were numerous small cysts in both plexuses. On cutting through the anterior portion of the fornix, the cyst, fornix, and choroid plexuses could all be turned back together. There was dilatation of both ventricles, but not to an extreme degree. The basal ganglia were normal. On making an incision into the cyst, after hardening, it was found to consist of a thin wall, within which was a clear hyaline substance firmly set by the re-agents in which it had been hardened.

Microscopical examination.—The cord and medulla were examined by the Marchi, Weigert-Pal, and Nissl methods. No degeneration or change could be found.

Nature of Growth.—The cyst was composed of three layers, an outer formed of elongated cells with rounded nuclei, closely packed together, making a fibrous-looking coat; a middle layer composed of large epithelial cells, like the prickle cells of the rete mucosum of the skin; and an inner layer of structureless tissue, forming the greater part of the tumour. The transition of the prickle cells into the hyaline tissue could be traced. (Cyst of the choroid plexus.)

EPILEPTIC ATTACKS WITH A WARNING OF A CRUDE SENSATION OF SMELL AND WITH THE INTELLECTUAL AURA (DREAMY STATE) IN A PATIENT WHO HAD SYMPTOMS POINTING TO GROSS ORGANIC DISEASE OF THE RIGHT TEMPORO-SPHENOIDAL LOBE.

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THE patient, A. B., a member of the medical profession, was 51 years of age, married, and of excellent health until three and a half years ago. He then had a severe attack of septicæmia, during the course of which an abscess formed in his anterior chest-wall and required to be opened surgically. From that illness he recovered and remained well until October, 1898, when he had a fresh septic infection in his right hand, which required several incisions. At that time his temperature was over 105° on several days and he was occasionally delirious. Since his second attack of septicæmia his general health has never been quite so good. There was no history of specific disease nor of any exposure to it. He never had any head injury nor had he, at any time, suffered from otorrhœa.

Ever since his second attack of septicæmia the patient had been subject to occasional attacks of excitement, without sufficient apparent cause. He used to come home from his rounds in a state of excitement. His general manner became different; his memory also became impaired, so that on several occasions he forgot important appointments. On one occasion he called to enquire for a patient who had long been dead.

About eight weeks before he came under our observation he began to have occasional attacks of nausea and what he called "giddiness," with frontal headache. In these attacks there was a strong sensation of smell, which he described as being "like camphor or ether." This smell was succeeded by what is commonly called an intellectual aura (dreamy state), in which—to use his own words—he "felt as if he were saying, doing, and looking at things which he had experienced before." He also stated that surrounding people seemed to have strange expressions on their faces, and that "people and things seemed to be far away" (he meant in physical distance). The average duration of each attack was about a minute; the patient's face, according to the account of a competent eye-witness of several seizures, one of which was very carefully observed throughout, was pale and his expression was that of one "facing an expected horror," but he was not apparently unconscious. No twitchings of face or limbs were ever observed. There was no vomiting either during or between the attacks.

After four weeks of such attacks, the crude sensation of smell ceased to occur, but there were numerous attacks, sometimes three in a day, of a slightly different type, in which he had nausea and vertigo. External objects did not appear to move, but the patient himself felt giddy, and he had a sense of fear and of impending death. Occasionally, during such an attack, he became momentarily unconscious and fell backwards. His face was always pale during an attack, and his pupils were dilated.

He never had diplopia, though six weeks after the commencement of his "attacks," when lighting a cigarette one day, he applied the lighted match to the cigarette-holder, apparently owing to some mental confusion.

His headache gradually became almost constant, the pain being both frontal and occipital, but within a week or so before he came under our observation the headache became less severe, and he seemed rather drowsy. Three weeks before, his left foot was noticed to drag a little in walking, but he could walk fairly long distances until he took to his bed, a week before we saw him.

His condition, on examination on September 11, 1899, was as follows:—He is a very intelligent man, able to answer clearly all questions put to him, though he seems somewhat drowsy; speech and articulation are normal. He can smell asafœtida and cloves in both nostrils, and names them. He can taste sugar and salt equally on both sides of the tongue, back and front. He hears a watch better in the right ear than in the left, and Mr. Ballance, on applying Weber's test, finds that the tuning-fork on the vertex is heard louder on the right side, all wax being previously removed from the right ear. The visual fields are normal on rough testing. There is no hemianopia on careful testing with small objects moved at the periphery of the visual fields, nor is there any obvious defective sight.

On ophthalmoscopic examination there is found well-marked neuritis of the right eye, with + 2 D of swelling there are no hæmorrhages; the left optic disc is red but not swollen. The pupils are equal in size, and react normally to light and during accommodation. The external ocular movements are normal. There is no squint, no diplopia and no nystagmus.

There is slight but distinct weakness of the left facial muscles, more marked in the lower than the upper part of the face. The left angle of the mouth is less energetically retracted and the left naso-labial fold shallower than on the right side. The left eye is less tightly "screwed up" by the orbicularis palpebrarum than on the right side when he is told to close both eyes as strongly as he can.

The palate rises normally on phonation. The tongue comes out straight on protrusion, but can be pushed better into the left cheek than into the right.

There is no anæsthesia anywhere on the face, trunk, or limbs to the lightest touches or pricks, but when the fingers of the left hand are touched and the patient is asked to point with his other hand to the exact point touched, his eyes being closed, he is several inches wide of the mark in every instance. There is no constant relation between the point touched and the position to which he refers the sensation.

The sense of position on passive movement is normal at all joints of the upper and lower extremities.

As to motor power, the patient can move all parts of the head, trunk and limbs as he lies in bed, but the left grasp is much weaker than the right. (L. = 30, R. = 63, with dynamometer.) There is no ataxia of the limbs and no tremor on voluntary movements.

The patient cannot stand alone; when supported he tends to fall backwards and slightly to the left side; in walking he scrapes the left foot very slightly on the ground.

The knee-jerks are normal and equal. There is no ankle clonus. The right plantar reflex constantly shows flexion of the hallux. The left side is sometimes flexion, at other times extension of the hallux. The sphincters are normal.

The lungs and heart are normal on physical examination;

the pulse is 70, regular, and of moderate tension. There is a scar of an old abscess on the front of the chest. The abdomen and urine are normal. The temperature is normal.

To-day, for the first time, he complains of unilateral headache, and indicates the right temporal region as the seat of pain. There is no tenderness on pressure or percussion over any region of the skull.

September 12.—During last night the respiration was of Cheyne-Stokes type, and the patient passed urine and fæces unconsciously. To-day he feels better and talks with perfect intelligence. The headache is less severe. His appetite is extremely good, and he can smoke cigarettes. The left facial weakness is more evident than yesterday. The pulse is 72, respiration 20 per minute. The knee-jerks are very faint, and can only be elicited by Jendrassik's method.

September 13.—During the night patient's temperature rose to over 100° F. He rapidly became comatose, and was observed to have occasional clonic spasms, confined to the left arm and hand. Death occurred at 1 a.m. from failure of respiration. The temperature at the time of death was not taken.

Unfortunately no autopsy could be obtained.

Summary.—To sum up the history of the case: the patient had gradually increasing mental dulness, followed nine months later by attacks of headache and nausea with a sensation of smell and a "dreamy state." Later the attacks changed in type. The paroxysmal smell ceased to occur, but there was occasional momentary unconsciousness. A few days before his death slight left hemiplegia developed, most marked in the face, without hemianopia or hemi-anæsthesia, but with some "cortical anæsthesia" of the left hand. There was some impairment of hearing in the left ear and optic neuritis in the right eye. Two days before death the headache became more localised and was referred to the right temporal region. The patient rapidly became worse and died from failure of respiration, slight jerking being observed in the left arm and hand just before death.

REMARKS BY DR. HUGHLINGS JACKSON.

I saw A. B. with Sir William Gowers about September 9, 1899. We concluded that there was disease, probably tumour, of one temporo-sphenoidal lobe. Sir William, from the right-sidedness of the optic neuritis, suggested before the setting-in of the left hemiplegia, that the right lobe was the one implicated. I saw A. B. again a day or two later, this time with Mr. Ballance and Dr. Purves Stewart. Mr. Victor Horsley also saw the patient. The question of operation was considered; it was decided not to operate.

It is very unfortunate that necropsy was not permitted, but the case is clinically a very important one, especially, I think, as exhibiting the association of a warning of a crude sensation of smell with the "dreamy state," and with the emotion fear, in slight epileptic seizures. The notes were taken by Dr. Purves Stewart. Dr. Stewart will remark on the question of localisation of the lesion, on the olfactory and paralytic symptoms, and on some other points.

I have published a case somewhat like that of A. B. (BRAIN, July, 1888, part xlii., p. 191), but unfortunately necropsy was not permitted; that case,[1] however, is one of great clinical interest. Dr. Stewart will mention other cases already published of epileptic fits with crude (warning) sensations of smell, cases completed by necropsies.

I have several times[2] written on the group of cases of epilepsy to which that of A. B. belongs; and have (*Lancet*, January 14, 1899), suggested for these cases the name of Uncinate Group of Fits; this was on the hypothesis that the discharge-lesions in these cases are made up of some cells, not of the uncinate gyrus alone, but of some cells of different parts of a region of which this gyrus is part—a very vague circumscription, I admit—the uncinate region. In cases of this group there is at the onset of the paroxysms a crude sensation of smell or one of taste, or there are movements of chewing, smacking of the lips, &c.,

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[1] The title given to the report of the case is a short summary of its symptomatology: "Epileptic Attacks with crude Sensation Warnings, by Smells and the 'Epigastric' Sensation, 'Intellectual Aura,' or 'Dreamy State.' Double Optic Neuritis. Attacks of Left-sided Tremor. Apoplexy and left hemiplegia. No necropsy."

[2] *Med. Times and Gazette*, vol. i., 1879; BRAIN, July, 1880; BRAIN, July, 1888; BRAIN (with Dr. Beevor), Oct., 1889; BRAIN (with Dr. Colman), Winter Number, 1898; *Lancet*, January 14, 1899.

(sometimes there is spitting). In some cases of this group there is a warning by what is known as the epigastric sensation, a crude development of a systemic sensation; this warning sometimes occurs along with a crude sensation of smell or with the chewing, &c., movements. Different varieties of this group of cases depend, I suppose, on discharge-lesions of different parts of what I call the uncinate region. As will have been inferred, it is supposed that especially in this cortical region, not confined to this region, are the physical bases of some of the systemic sensations—the physical bases of those systemic sensations which, to speak very roughly, especially appertain to the digestive system.

Many of the symptoms of even slight paroxysms of uncinate fits depend, of course, on discharges wide-spread beyond, some far beyond, the uncinate region—depend on discharges *secondary* to the *primary* discharge, that of the discharge-lesion.

There is the dreamy state in the paroxysms of many, not of all, cases of the uncinate group of epileptic fits.

I hope soon to be able to write more fully on the uncinate group of epileptic fits. I shall then consider exceptions to the statements made in the preceding paragraph, and shall re-enquire particularly as to the relation in slight epileptic paroxysms of crude auditory sensations to the dreamy state.

A. B. had only slight epileptic attacks, *le petit mal*, and two degrees of them; in the slightest of his slight attacks he had crude sensations of smell and the dreamy state; in the severer of his slight attacks there was "unconsciousness" without the crude sensation and without the dreamy state.

The dreamy state in the uncinate group of epilepsies varies very much in different cases.[1] In A. B. it was the peculiar intellectual state which many healthy people or people slightly out of health have occasionally—Reminiscence.

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[1] As I have said, the dreamy state does not occur in the paroxysms of every case of the uncinate group, and I now say, too, that the dreamy state may, according to statements of patients and their friends, occur without any one of the crude sensations I have mentioned in the text, and without the chewing, &c., movements.

It is quite evident that in some slight epileptic paroxysms with the dreamy state—in all of them, I believe—there is a kind of double consciousness—a "mental diplopia." In a quotation from Herpin (*vide infra*) will be found clear evidence of "mental diplopia" in several of the cases he mentions. I think, too, that there is probably some defect of consciousness in every paroxysm with the dreamy state; certainly there is in some of them. The psychical condition, therefore, is a very complex one. There is defect of consciousness, so far negatively. Positively, there is (1) the quasi-parasitical state of consciousness (dreamy state), and (2) there are remains of normal consciousness; and thus (1 and 2) there is double consciousness. To discover the physical conditions correlative with this complex psychical condition is a very difficult task. There was also an abnormal[1] emotional state in some at least, of A. B.'s severer slight attacks—fear, *and a sense of impending death;* in the slighter of his slight attacks there was an expression of "one facing an expected horror" (*see* Herpin, *Des Accès*, &c., p. 111, quoted at the end of these remarks). I have said, *Med. Times and Gazette*, March 1, 1879, that the epigastric sensation in epileptic paroxysms is often accompanied or quickly followed by the emotion fear. Sir William Gowers thinks that this association is very rare. A. B. had no epigastric sensation warning.

We must not, in this part of our investigation of epileptic paroxysms, limit enquiry to the symptom fear; we have to take heed of all departures from the patient's "ordinary state of feeling." And it must be well borne in mind that the departure in uncinate paroxysms is in some cases towards a more pleasurable, although more often towards a more disagreeable, state. Further, what is obviously equally significant, early in the course of a case of epilepsy the feeling in the slight paroxysms may be pleasurable, and, later, disagreeable—differences depending probably on the degree and rate of the discharge of the discharge-lesion.

The symptom at the onset of A. B.'s attacks—that external objects seemed to be far away—deserves careful attention.

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[1] I say abnormal because, of course, I do not mean the natural fear of the fit itself, but a fear which "comes by itself"—the *symptom fear*.

In, or before, or after some slight paroxysms of cases of the uncinate group, there are gastric or intestinal symptoms, or both.

To speak very roughly, much of the symptomatology of uncinate fits refers very especially to the digestive system; the crude sensations, smell, taste, and the epigastric sensation are, to speak with brutal disregard of psychological propriety, crude developments of "digestive sensations."[1] In what, for reference, I will call Herpin's "third smell case" (*vide infra*), there were in the patient's paroxysms crude sensation of smell, abnormal intellectual and emotional states, and gastric spasm. The dreamy state, an abnormal intellectual state, is not a "digestive symptom," nor is an abnormal emotional state. But the occurrence in healthy people of gastric and intestinal states, things physical, along with the psychical states, pleasure and pain, is known to everybody ("bowels of mercy," &c.). The occurrence of gastric and intestinal symptoms in some cases of uncinate fits with abnormal emotional states is obviously significant.

I take this opportunity of advising the younger medical neurologists to study carefully Herpin's writings on Epilepsy. I have long known his valuable work, *Du Pronostic et du Traitement Curatif de l'Epilepsie*, 1852, but I have only recently heard of his still more valuable work, *Des Accès Incomplets d'Epilepsie*, 1867. I give, from the latter work, a quotation which mentions one case of the association of an intellectual aura ("dreamy state") with a crude sensation warning of smell in epileptic paroxysms ("third smell case").

Among three hundred cases of epilepsy observed by Herpin there were three, the paroxysms of which began by a warning of smell. In the report of only one of these three (I called it Herpin's "third smell case") is what I take to be a "dreamy state" ("tristes souvenirs"—"un trouble intellectuel") mentioned; the patient's emotional state in her paroxysms, from the description Herpin gives in the words I italicise, was similar to that A. B. had ("sense of fear and of impending death") in those of his paroxysms in which he lost consciousness. Herpin writes, *Des Accès Incomplets d'Epilepsie*, pp. 115 and 116, 1867:—

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[1] Although smell takes low rank as it serves as a "digestive sensation," it has very high rank in another way. It has been called the most suggestive of all the senses; and smells have remarkable power in calling up remembrances of past scenes. We must, however, for several reasons, not be hasty in concluding anything from this with regard to explanations of the nature of the association of crude sensations of smell with the dreamy state in slight epileptic paroxysms.

"L'un de trois malades à début par de fausses perceptions d'odeurs perdait si vite connaissance qu'il ne pouvait que rarement avertir. Un autre sentait l'odeur descendre dans la gorge; alors toute perception se perdait. La troisième éprouvait une sensation qui de la gorge descendait dans l'estomac où elle se convertissait en inquiétude et en tortillements; pendant ce spasme, de tristes souvenirs assiégeaient la patiente; *il lui semblait qu'elle allait mourir;* aussi, quoique l'odeur fût agréable, l'impression qu'elle en éprouvait [était] des *plus pénibles*, mais bientôt elle perdait ses sens.

"Dans les débuts par l'organe olfactif, l'abolition de la conscience suivait donc le plus souvent le prélude; dans un cas, celui-ci était suivi d'un *spasme gastrique précédant un trouble* intellectuel pendant lequel la connaissance se perdait."

In the following quotation from p. 140 *op. cit.*, Herpin mentions a case so similar to the third case mentioned in the foregoing quotation from pp. 115 and 116, that, I think it is the same case—that there is, in one of the two reports (pp. 115 and 140), some mistake in the words which indicate sex.

"De trois patients à début par de fausses perceptions d'odeur, deux n'avaient pas d'accidents moindres que les vertiges. Le troisième avait quelquefois de simples preludes; la mauvaise odeur ne s'étendait pas au de là des fosses nasales (tandis que dans le vertige la sensation descendait dans la gorge); bientôt tout était fini; il n'y avait pas trace de trouble intellectuel; il appelait ces accidents légers 'ses *mauvaises odeurs*.'" In this third case (supposing it to be the same as the third case Herpin mentioned, pp. 115 and 116), the paroxysms were sometimes very slight indeed, simple preludes; there were then crude sensations of smell without the "trouble intellectuel"; in somewhat stronger slight fits there was the "trouble intellectuel" also—differences due to differences in the degree of "intensity" of the primary discharge, that of the discharge lesion, and consequent differences in the range of the induced (secondary) discharges of the normal nervous elements with which the fulminant cells of the discharge lesion were connected.

I have several times drawn attention to the importance of taking careful note of chewing, &c., movements in epileptic paroxysms; they occur in one variety of uncinate fits, and sometimes there is, as in the other varieties, the dreamy state with them, and sometimes, as in the other varieties, there are elaborate actions during so-called unconsciousness after such seizures. There were no such movements in A. B.'s paroxysms.[1] I published (with Dr. Colman) a case in which there were such movements in the epileptic paroxysms of a patient who had the dreamy state (case of Z., BRAIN, Winter Number, 1898), small focus of, or relics of, softening in the left uncinate gyrus. As I have several times mentioned, I consider in accord with certain of Ferrier's inferences from experiments on the monkey, that these movements signify—are indirect consequences of—epileptic discharges of cortical gustatory elements. I quoted an account of an epileptic paroxysm with these movements (mâchillement, &c.) *Lancet*, January 14, 1899, from Herpin's *De l'Epilepsie*, p. 275, 1852; there is in Herpin's report of that case no mention of a dreamy state. I now give a quotation from Herpin's other work, *Des Accès*, &c. I do so to impress on the younger medical neurologists the great importance of observing a symptom which at first thought may seem to be of little value.[1]

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[1] Most neurologists will have read the report of a very remarkable case published by Dr. Mesnet (*L'Union Medicale*, Juillet 21 et 23, 1874), a case of what he calls "Pathological Somnambulism." I draw attention to the words of Dr. Mesnet, which I have italicised in the subjoined quotation.

He writes of his patient: Sa démarche est facile, son attitude calme, sa physionomie paisible; il a les yeux largement ouverts, la pupille dilatée; le front et les sourcils contracturés, avec un mouvement incessant de nystagmus accusant un état de malaise, de souffrance vers le tête; *et un mâchonnement continu.*" There is no mention of a dreamy state, and it appears that the "mâchonnement" was not at the onset of the paroxysms only

This case is remarked on by the late Professor Huxley in an article "Animal Automatism" ("Collected Essays," vol. i.). The case has also been remarked on by Azam (Tuke's "Dict. of Psych. Med.," article, "Double Consciousness"), and by the late Hack Tuke, in his work on Somnambulism. Huxley alone mentions the "chewing motion of the jaws."

Without expressing any opinion as to the nature of the case Dr. Mesnet reports, I may say that I have notes of cases in which after epileptic fits which began by chewing, &c., movements, or by a crude sensation of smell, there have been post-epileptic actions of great elaborateness during so-called unconsciousness.

Herpin wrote, *Des Accès Incomplets d'Epilepsie*, pp. 150-1, "En étudiant les débuts des attaques, nous avons décrit les symptômes qui se lient a ce spasme [le spasme pharyngé] sous les noms de mâchonnements, de mastication, de gustation, de déglutition, nous ne répéterons pas cette description, mais nous devons insister sur le fait *que ces signes sont précieux pour le vertige comitial qu'ils distinguent du vertige ordinaire d'une syncope* légère, d'un faible accès hysterique, &c. (No italics in original.) Ces phénomènes sont, chez quelques épileptiques, tellement caractérisés et constants, que les patients, au lieu de donner aux accès incomplets dans lesquels il se montrent, les noms, en quelque sorte génériques, d'absences, d'étourdissements, de fausses attaques, &c., les appellent *mouvements de bouche, mâchonnements, mâchillements, rincements de bouche*." (Italics in original.)[2]

I give also part of what Herpin wrote on *perturbations de l'intelligence* (commonly called intellectual auræ), which I call dreamy states. It is a pity that he did not mention the particular "hallucinations" some of the patients had; I imagine these "hallucinations" were what I call crude sensations.

"Pour dix patients le début consistait en des *perturbations de l'intelligence*, avec ou sans hallucinations. Des exemples peuvent seuls donner une idée juste de ces aberrations; une malade d'un esprit très-distingué nous disait: 'Il s'agit d'un trouble purement intellectuel; je n'ai ni éblouissements, ni vertiges, je puis lire encore les mots, mais je n'en comprends plus le sens. C'est un état des plus pénibles; il me semble qu'une partie de mon intelligence assiste à l'égarement de l'autre.' . . . Un jeune prêtre de grande espérance s'exprimait ainsi: 'Ce sont des idées sans suite et cependant contradictoires; si j'entends une conversation, elle me suscite deux idées qui se combattent; je perds la tête et non pas la connaissance; j'entends, je comprends, mais mon esprit est ailleurs.' Autre version d'un autre patient: 'Il y a en moi deux personnes dont l'une jouit de la raison et l'autre déraisonne.' Un épileptique parlait d'une idée fixée, toujours la même, mais qu'il n'a jamais pu se rappeler. Un autre mentionnait seulement un égarement de la raison. Une jeune personne d'un esprit très-observateur racontait ainsi le début de ses attaques: 'Je suis prise, sans cause, d'une tristesse subite, et a l'instant même mes yeux restent fixés sur un objet et ma pensée sur une idée qui me rappelle l'image très-nette d'un ancien rêve; l'idée fixe m'absorbe tellement que, quoique je regarde toujours vers le même point, je ne vois plus l'objet.'"—*Des Accès Incomplets d'Epilepsie*, 1867, p. 111.

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[1] I do not think, I may say here, that Herpin distinguishes between what we now call the epigastric sensation warning and warnings by gastric spasm.

[2] One of my patients who had such movements at the onset of slight epileptic attacks (no dreamy state, but a temporary very elaborate quasi-somnambulistic state after his seizures), in a letter to me, spoke of his fits as "champing fits."

One reason for giving these quotations is that some of the symptoms I have mentioned here and in other papers as occurring in some slight epileptic paroxysms, seem so odd that the reports of the cases may appear to some medical men more like collections of scientific curiosities than things with practical bearing. I wish to show by the quotations from Herpin that statements essentially the same as those I make were made by a great authority long ago. I will here quote from a former article, BRAIN, July, 1888, p. 187.[1]

"Before leaving this part of my subject, I remark, by way of recapitulation, that he who neglects the 'dreamy state,' because it is indefinite and 'merely curious,' and such symptoms as chewing, &c., movements, and apparent alteration in the size and distance of external objects, because they seem trifling things, may not even surmise that his patient has the serious disease, epilepsy, in a rudimentary form, until a severe fit comes to tells him so."

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[1] "On a Particular Variety of Epilepsy ('Intellectual Aura'): One case with Symptoms of Organic Brain Disease."

REMARKS BY DR. PURVES STEWART.

In the above case the history of gradual mental impairment followed by attacks of unconsciousness, together with the presence of headache, of optic neuritis, and of slight hemiplegia, pointed to the existence of gross intra-cranial disease. The left-sided weakness, most marked in the face, but also distinct in the arm and leg, indicated clearly as the site of the lesion some part of the motor tract, or of its vicinity, in the right cerebral hemisphere. The absence of hemianæsthesia and of hemianopia showed that the lesion was probably not in the neighbourhood of the internal capsule, but that it was situated more towards the cortex of the brain, a view which strengthened by the presence of "cortical anæsthesia" of the left hand. The occurrence of Babinski's extensor plantar reflex—extension of the hallux instead of the normal flexion, on tickling the sole of the foot—was not sufficiently constant to be of much significance.

The peculiar nature of the paroxysms, and especially their association with a sensation of smell, pointed to some abnormal condition of the temporo-sphenoidal lobe.

Drs. Hughlings Jackson and Beevor[1] record the case of a sarcoma, the size of a tangerine orange, situated at the most anterior extremity of the right temporo-sphenoidal lobe. During life the patient had left hemiplegia without hemianopia, hemianæsthesia, or affection of smell, taste, or hearing. She also had numerous fits with an "intellectual aura" and a "horrid smell of dirty burning stuff."

Drs. Hughlings Jackson and Colman[2] also record a case of a small subcortical patch of softening in the left uncinate gyrus. The patient had been subject to epileptic attacks accompanied by a "dreamy" state, with smacking movements of tongue, lips, and jaw, but without crude sensations of taste or smell.

Dr. James Anderson[3] published a case of a large basal cystic sarcoma arising from the pituitary body and spreading into the left temporo-sphenoidal lobe. It had given rise to attacks of peculiar sensation in the right hand, preceded by a sensation of a bitter taste in the mouth, with occasionally also a peculiar smell, and accompanied by the "dreamy state." There were never any chewing or smacking movements of the lips. Smell was impaired on the left side, and there was slight defect of taste on both sides, especially the left. From affection of the left optic nerve, optic chiasma, and optic tract, the patient had blindness of the left eye with temporal hemianopia in the right.

Mr. Nettleship[4] also records a case of tumour of the pituitary body implicating the left optic nerve, chiasma, and tract, as well as the left temporo-sphenoidal lobe. In that case there had been paroxysmal sensations of suffocation in the nose and mouth. There is no mention of a dreamy state in that case.

Sanders[5] records a case of a large glioma on the under surface of the brain, involving the anterior part of the left temporo-sphenoidal lobe and the lower convolutions of the left frontal lobe, and destroying the left olfactory tract. The patient had fits, preceded by a warning of a "dreadful disagreeable smell," also chewing movements of the jaw and spitting of saliva. Later he had convulsions affecting the face, but not the limbs. No dreamy state was recorded in that case.

Dr. McLane Hamilton[6] also published a case of localised chronic pachymeningitis affecting the right uncinate gyrus and part of the adjacent convolutions, but without involvement of the olfactory bulbs. The patient had been subject to attacks, preceded by a peculiar disagreeable odour, either of smoke or of a fœtid character. No mention was made of any dreamy state.

In our case of A. B. the view as to the localisation of the disease in the right temporo-sphenoidal lobe was further supported by the impairment of hearing in the left ear without any discoverable cause in the ear itself, and, therefore, possibly referable to some slight affection of Ferrier's auditory centre on the side of the lesion.

The slight "cortical anæsthesia," the slight hemiplegia, most marked in the face, together with the occurrence of localised fits in the left arm and hand before death, are facts which, so far as they go, indicate either that the lesion was not confined to the temporo-sphenoidal lobe alone, and extended to the lower central convolutions so as to affect the face and arm centres, or, more probably, that it pressed upwards in that direction.

The absence of an autopsy unfortunately leaves undetermined the exact nature and limits of the lesion. On the whole, the slow course and progressive march of the symptoms indicate that it was a new growth of some sort. The history of septicæmia rendered it conceivable that a chronic abscess might have been present. Mr. Ballance informs us that he has known a brain abscess to lie latent for fifteen months after an attack of septicæmia, without previous otorrhœa or other apparent local exciting cause, at the end of which period symptoms appeared for the first time, and rapidly proved fatal. But in A. B.'s case the symptoms were those of a lesion involving not only the temporo-sphenoidal, but also the lower central region, and this with very slight motor weakness, less in amount than an abscess of such size would have been likely to produce. It is, therefore, more probable that there was an infiltrating growth involving the temporo-sphenoidal lobe and the adjacent part of the "central" region. This, however, is mere hypothesis, and the absence of an autopsy is much to be regretted.

Amongst other points of interest in the case is the unilateral optic neuritis present on the side of the cerebral lesion. Mr. Marcus Gunn,[7] in a discussion on the diagnosis of brain tumours, states that unilateral, or preponderatingly unilateral, neuritis is, on the whole, in favour of the tumour being on the same side as that on which the neuritis is more intense, if other reasons exist for localising the tumour far forward in the brain. Our patient's case, so far as it goes, seems to bear out Mr. Gunn's views. But the rule is not an invariable one, for I have seen a case of a large frontal tumour in which the optic neuritis was both earlier and more intense on the opposite side from the lesion.

The remarkably large appetite, which our patient exhibited up to the last, is of interest when considered with a case of temporo-sphenoidal abscess and a series of cases of head injuries published by Mr. Stephen Paget,[8] in which voracious hunger or thirst were outstanding symptoms.

REFERENCES.

(1) Brain, vol. xii., 1889, pp. 346-357.
(2) Brain, vol. xxi., 1898, pp. 580-590.
(3) Brain, vol. viii., 1886.
(4) *Ophth. Soc. Trans.*, vol. iv., p. 285.
(5) *Archiv f. Psychiat.*, vol. iv., 1874, p. 284.
(6) *New York Medical Journal*, 1882, vol. xxxv., p. 575.
(7) Brain, vol. xxi., 1898, p. 337.
(8) "Essays for Students," 1899, pp. 92-100.

REMARKS ON LOSS OF MOVEMENTS OF THE INTERCOSTAL MUSCLES IN SOME CASES OF SURGICAL ANÆSTHESIA BY CHLOROFORM AND ETHER.

BY J. HUGHLINGS JACKSON, M.D., F.R.S.

AND

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PART I.[1]

IN the *Lancet*, January 2, 1897 (Neurological Fragments, No. 17), I mention, in a footnote, the condition of the respiratory apparatus in some cases of surgical anæsthesia. A few years ago, Dr. Howard Sturge, my then house physician at the London Hospital, told me he had observed that a woman's breathing became abdominal when she was under chloroform. (By abdominal breathing in this note is meant respiration in which the diaphragm acts without the co-operation of the intercostal muscles, there being no respiratory movements of those muscles.) I have, since hearing Dr. Sturge's remark, observed abdominal breathing during surgical anæsthesia in several cases, both in men and women; the abdominal breathing is more striking in women because their normal respiration is chiefly costal. I learn from Dr. Hewitt's very interesting work "Anæsthetics and their Administration," p. 219, that "Snow stated that thoracic movements usually cease before the abdominal." (Dr. Hewitt is speaking of an over-dose of chloroform.) Abdominal breathing occurs in some cases of coma (apoplexy) in men and women from other causes than chloroform and ether.

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[1] This part is written by J. H. J.

In many cases of apoplexy the breathing is mainly costal, the epigastrium sinking in inspiration. Probably the manner of respiration differs much according to the stage of coma in apoplexy as it does according to the stage of surgical anæsthesia. In this note I speak only of abdominal breathing in the coma of surgical anæsthesia. I much regret that I have not noted in all the cases I have observed, whether the anæsthetic used was chloroform or ether, or some mixture of anæsthetics.

Whether the breathing becomes abdominal or not probably depends most on the degree of the anæsthesia. I will mention two cases in illustration of this remark. I saw with Mr. Ballance and Dr. Collier a girl, 19 years of age, who had chloroform for a short examination (functional affection of one hip); during the anæsthesia her intercostals acted in normal fashion during respiration. I suppose the anæsthesia in this case was not nearly so deep as that in the following: I saw a young man made deeply anæsthetic with chloroform by Dr. Dudley Buxton for an operation of trephining the skull by Mr. Horsley; in this patient the intercostals did not act; abdominal breathing was well marked and great, the diaphragm being in vigorous action. We have to consider stages of anæsthesia. I have seen the breathing almost solely costal in men anæsthetised; possibly this was in an early stage of their anæsthesia. Dr. Collier will remark on this part of our subject.

In cases of surgical anæsthesia where the intercostal *muscles* do not act, there is, at any rate, loss of their respiratory *movements*. This may seem rather an absurd remark. But there are, I submit, non-respiratory as well as respiratory movements of these muscles. I have (N. F., No. 15, *Lancet*, February 23, 1895) drawn attention to the difference between their respiratory movements on the one hand, and their "voluntary" (cerebral, non-respiratory) movements on the other hand. In another note (N. F., No. 12, *Lancet*, December 22, 1894) I published a case (of supposed pneumonia) in which there was loss of the respiratory movements of the intercostal muscles with possibility of perfect "voluntary" (cerebral, non-respiratory) movement of those same muscles. In that case these muscles did not act at all in the patient's respiration proper; his breathing was abdominal, and yet acted quite well in the "voluntary" (cerebral, non-respiratory) movement of drawing in his breath when told, the so-called (mis-called) "forced *inspiration.*" I suggested (N. F., No. 12) that in this case there was loss of function, produced by pneumo-toxin, of the lateral horns of the cord (some centres of the costal part of what I call the Lowest Level of the central nervous system), from which resulted loss of the *respiratory* movements of the intercostal muscles; a further suggestion was that there was integrity of the remainder of the (costal) anterior horns, so that upon cerebral instigation this remainder acted effectually on the intercostal muscles in the "voluntary" movement of drawing in the breath, expanding the chest on command—a non-respiratory movement. It is possible that in the abdominal breathing of deep surgical anæsthesia from chloroform or ether, the lateral horns are affected earlier than, and that they are affected more than, the remainder of the anterior horns. But it is not likely that we could show that in these cases the remainder of the anterior horns is intact or but little affected, because no "voluntary" (cerebral) movements, ordinarily so-called, can, in the circumstances, be instigated from the cerebral cortex. Yet a patient may call out loudly when under chloroform or ether. In normal circumstances such calling out would imply prior inspiratory movement of the upper chest; rather, I ought to say (since drawing in the breath prior to vocalisation is a "voluntary," at any rate, a cerebral movement), it would imply expansion of the chest; it does not follow, however, that in surgical anæsthesia the movement prior to the vocalisation of calling out loudly, supposing there to occur such a movement, is costal; it may be diaphragmatic. It may be well to observe whether a movement of the intercostals for *expanding the chest* can occur in a patient so deeply anæsthetic by chloroform or ether that the *respiratory* movements of these muscles are lost. It will, however, most likely be held that the *quasi-voluntary* movement mentioned could not occur in so great a depth of surgical anæsthesia as that in which the *respiratory* movements of the intercostals are lost. There is something more to be said here. Dr. Collier allows me to borrow from his remarks (see Part II.) what he writes on the case of a child deeply anæsthetised and breathing only with the diaphragm, that is in a condition in which the intercostals did not act in respiration. Dr. Collier writes: "When the operation was commenced the patient uttered two or three groans, each being preceded by an inspiratory movement in which the elevation-expansion movement of the chest was very marked."

There is another possible cause of loss of the movements of the intercostal muscles in deep anæsthesia to be considered. The late Dr. Franklin Hooper, of Boston, stated in a paper read before the American Laryngological Association, in 1885, that (now I quote from a lecture by Sir Felix Semon, *Brit. Med. Journal*, January 1, 1898), "stimulation of the recurrent laryngeal nerve, uncut or cut, with an electric current, which throughout was kept equally strong, resulted in adduction of the corresponding vocal cord when the narcosis—he always employed ether—was slight; whilst, when the anæsthetic was pushed to the condition of very deep narcosis, stimulation with a current of the same intensity resulted in decided abduction of the corresponding cord. This very extraordinary fact has, I am afraid, never met with the attention it deserves, although Mr. Horsley and I ('On an apparently Peripheral and Differential Action of Ether upon the Laryngeal Muscles,' *Brit. Med. Journal*, 1888) have specially pointed out its importance, after having convinced ourselves, by repetition of Dr. Hooper's experiments, of the correctness of his statements. The fact that the result of electrical stimulation—currents of the same strength being used throughout—entirely differs according to the depth of the narcosis, not only when the entire recurrent, but also when, after its section, its peripheral end is stimulated, clearly points to the conclusion that the difference cannot be due to any differentiating influence of the anæsthetic agent upon the nerve centres, but that there must be a specific peripheral and differential action on its part, through the agency of the circulation, upon either the nerve-fibres, the nerve-endings, or the muscular substance itself. In other words, there must be biochemical differences between the two antagonistic apparatus, which in all probability some day will explain the fact of the greater vulnerability of the abductors as compared with the adductors."

So it is possible that in deep surgical anæsthesia the inaction of the intercostal muscles may be partly or mainly or solely owing to action of the drug upon the muscular tissue of the intercostals or on motor nerve endings in these muscles. If the intercostals are fully paralysed by such local action of ether, they could not act in any way, neither respiratorily nor in any possible quasi-voluntary expansion.

In chronic cases of disease of the nervous system paralysis of the intercostal muscles may be overlooked. This paralysis, at least if it develops slowly, does not seem to trouble a patient who is obliged to keep his bed by paralysis of the limbs or by other equivalent incapacity. I am not sure that some important characters of paralysis of the intercostal muscles are widely enough known. We must bear in mind that (Duchenne) the diaphragm can by itself, that is, I mean can, when the intercostal muscles are paralysed, raise and evert the lowest ribs. These ribs, diaphragmatic ribs Duchenne calls them, always move as mentioned, so far as I have yet seen, in cases of paralysis of the intercostal muscles from disease or injury of the spinal cord (with perhaps one exception in an infant), as well as in cases of that paralysis in surgical anæsthesia; they acted vigorously in the case of Mr. Horsley's chloroformed patient (*vide supra*). Action of the lowest ribs in these cases does not show, as the inexperienced might suppose, that the lowest intercostal muscles have escaped paralysis, and that only the upper ones have suffered. Faradisation of the phrenic nerve causes, among other effects, eversion and raising of the lowest ribs.

I think paralysis of the upper intercostals may be partly masked in surgical anæsthesia by great over-action of the scalene muscles. In a man deeply etherised by Dr. Buxton the diaphragm acted vigorously; the lowest and middle parts of the sternum sank in inspiration, but the sides of the uppermost parts of the chest did not; in this case however the scalene muscles were in very great activity (the diaphragm and scalene muscles can act together in concertina fashion).

It must be well borne in mind that the upper chest wall does not stand still in all cases of paralysis of the intercostal muscles; in young people it may move a great deal. But in these cases the upper chest during respiration moves in a wrong way; it sinks in inspiration—sinks when it should rise—sinks when the diaphragm acts; so to say, the upper chest is "sucked in" in inspiration. The movement of the upper chest after this one of "sucking in"—the movement of the upper chest during relaxation of the diaphragm—is only recoil, and is in the opposite direction of the normal recoil in the expiration of the healthy. There is no muscular action of the intercostal muscles in either the "sucking in movement" or in the "return" movement, that by recoil. In some cases of this kind when respiration is rapid paralysis of the intercostals may not be easy to determine; the upper chest moves up and down very frequently, and the timing of its motions with the equally frequent actions and relaxations of the diaphragm may be difficult.

As to the mode of action of the diaphragm in causing movements of the lowest ribs, either in health or in cases of paralysis of the intercostals, I say nothing in this paper. I quote the following from Dr. G. V. Poore's "Selections from the Works of Duchenne," p. 325 (the reference is to Duchenne's *L'Electrisation Localisée*, 3rd ed., pp. 901-921):—

"(*A*) *Diaphragm*. . . . (1) My experiments on men and animals show that the contraction of the diaphragm caused by electrifying the phrenic nerve, isolated or otherwise, from its nervous connections (communiquant ou non avec l'arbre nerveux) causes an elevation and outward movement of the diaphragmatic ribs as long as the abdominal walls are intact. The antero-posterior diameter of the base of the thorax is also slightly increased. In some cases the outward movement of the lower ribs is communicated to the upper.

"This observation has been confirmed by clinical experience.

"(2) If the belly be opened and the bowels pulled downwards the contraction of the diaphragm by itself causes an *inward* movement of the diaphragmatic ribs."

I have not observed the movements of respiration of patients deeply under chloroform during the operation of abdominal section for the removal of large cysts, &c., and do not know whether in these cases the lowest ribs evert and rise or turn in.

I suggested to Dr. James Collier a further research on the respiratory condition during anæsthesia by ether and chloroform. An account of his observations follows.

PART II.[1]

At Dr. Hughlings Jackson's suggestion I have examined the respiratory movements in sixty patients, before and during the administration of anæsthetics for surgical purposes. Twenty-five of these patients were children, fifteen were male adults, and twenty female adults. In a few cases a graphic record of the thoracic and of the abdominal movements throughout the period of the administration of the anæsthetic was taken by means of two recording stethographs, one placed round the thorax and one round the abdomen. The anæsthetics used were chloroform or ether, and in one case first ether and then chloroform was administered. I am indebted to the kindness of Mr. Stansfield Collier for the opportunity of examining children during his operations at the Hospital for Sick Children, Great Ormond Street. The results obtained are here summarised.

(1) *Chloroform anæsthesia.*—During the initial stages of the anæsthesia the respiratory movements were increased in range and in frequency, and were either of the same type as before the administration of the anæsthetic or were more preponderatingly thoracic, and this increase of range and frequency persisted until the struggling ceased. The respiratory movements then slowly became of less range, and the

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[1] This part is written by J. S. C.

elevation-expansion movement of the chest gradually became less and less, while the abdominal movement was more marked than before the anæsthetic was commenced.

At the period when the corneal reflex was no longer obtainable and when the anæsthesia was complete, the condition of the respiratory movements was generally as follows: —The elevation-expansion movement of the chest was very slight, while the abdominal (diaphragmatic) movement was well marked. In the female patients this condition contrasted most strikingly with the normal preponderatingly thoracic type of their respiratory movements.

After deep anæsthesia had lasted some time—a period which varied greatly with the individual, but which was on an average about fifteen minutes—the elevation-expansion movement of the thorax disappeared, though the scalene muscles still appeared to be in action, to a slight extent, in inspiration. Respiration was, with this exception, entirely abdominal. The eversion of the lower ribs in inspiration by the diaphragm was marked. The movement of the upper two-thirds of the chest alternated with the abdominal movement, the chest sinking in inspiration and rising in expiration. With a continuance of deep anæsthesia all trace of action of the scalene muscles disappeared. The diminution or cessation of the elevation-expansion movement of the chest seemed dependent, not upon the mere depth of the anæsthesia, but upon the time which deep anæsthesia had lasted. In these cases, after the anæsthetic was discontinued, the first elevation-expansion movement of the chest was noticed in the sigh of returning consciousness, after which the respiratory movements soon returned to their normal state. In cases where facial respiratory movements (action of dilatatores narium in inspiration) were present, such movements were lost early in the anæsthesia, generally just before the loss of the reflexes. In cases where the anæsthesia was of brief duration, though sufficiently deep for minor surgical procedures, very little diminution of the expansion movement of the chest in inspiration was noticed. A similar result obtained in subjects addicted to alcohol, and in these patients, even after prolonged deep anæsthesia, the elevation-expansion movement of the chest on inspiration was not lost, but only diminished. The susceptibility of different individuals to chloroform, as evidenced by the change in the character of the respiratory movements, seemed to vary greatly.

(2) *Ether anæsthesia.*—The results obtained were similar to those obtained with chloroform, with this important difference, that the elevation-expansion movement of the thorax in inspiration, though much diminished after prolonged ether anæsthesia, was never completely lost in any case that I have had the opportunity of examining. In one case, after deep anæsthesia had been kept up by ether for twenty minutes, the expansion of the chest in inspiration was still obvious. Chloroform was then substituted for the ether, with the effect that in about two minutes the expansion movement of the chest in inspiration became completely lost.

(3) *Chloroform anæsthesia in children.*—The observed cases seemed to fall into three groups, according to the length of administration of the anæsthetic and the susceptibility of the individual.

(a) The elevation-expansion movement of the chest was greatly lessened, but was still present throughout the anæsthesia. (Brief anæsthesia.)

(b) The diaphragmatic movement and the elevation of the upper chest by the scaleni was marked. Sinking in of the supra-clavicular and supra-sternal fossæ was marked. This seemed to be due to an increased action of the scaleni, the first rib being drawn up farther than in normal respiration, and so making these fossæ deeper. The expansion of the chest, except that produced upon the lower ribs by the diaphragm was lost. The middle region of the chest sank passively during inspiration, the scaleni and diaphragm acting upon the thorax in concertina fashion. (Deep anæsthesia.)

(c) The inspiratory movement was solely diaphragmatic, the only thoracic movement being a slight raising and an eversion of the lower ribs. The abdominal inspiratory movement was accompanied by passive sinking of the chest and the expiratory movement by recoil expansion of the

chest. (Deep and prolonged anæsthesia.) In two cases of this group, the anæsthesia was apparently deep and the corneal reflex was lost. The diaphragm was alone in action in the respiratory movement. When the operation was commenced the patient uttered two or three groans, each being preceded by an inspiratory movement in which the elevation expansion movement of the chest was very marked.

The action of the diaphragm upon the lower ribs.—By the kindness of Dr. Voelcker I have had the opportunity of examining the action of the diaphragm and the effect of its contraction upon the lower ribs in a case where the abdominal *point d'appui* of the diaphragm had been removed by an extensive abdominal incision and the removal of a very large ovarian cyst. Duchenne[1] has proved that contraction of the diaphragm raises and everts the lower ribs, and, relying upon experimental simulation of the phrenic nerves in animals, states that the diaphragm only elevates the lower ribs so long as it is supported by the abdominal viscera and parietes, and that when, in one of the lower animals, the abdomen is eviscerated, contraction of the diaphragm is accompanied by depression and drawing-in of the lower ribs; and he rejects the opinion of Beau and Massiat[2] that the pericardium, &c., can afford a more or less fixed point from which the diaphragm can raise the lower ribs in its contraction.

In Dr. Voelcker's patient, a girl of nine years old, a laparotomy was performed for abdominal tumour, and an ovarian cyst, the size of a large melon, was removed.

Before the anæsthetic (chloroform) was commenced, the respiratory movements were preponderatingly thoracic, and some diaphragmatic movement, with eversion of the lower ribs during inspiration, more marked on the left side, occurred. When anæsthesia was complete the scalenes and diaphragm alone acted, the "concertina action" of the thorax being marked.

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[1] *Physiologie des Mouvements*, 1867, p. 632.

[2] "Recherches sur la respiration," *Arch. genér. de Med.*, 4e série, t. ii., Art. 3e.

A long incision was made in the middle line of the abdomen and the tumour turned out of the abdominal cavity whole, and removed, its pedicle being ligatured. The intestines were collapsed, and the abdominal walls were quite flaccid.

In this condition the eversion of the lower ribs during inspiration was very marked, although the upper ribs sank during inspiration, and this continued so long as the patient was observed. According to Duchenne's explanation of the mode of action of the diaphragm in raising the lower ribs the reverse should have happened, as the anatomical conditions were similar to those in his experiments upon eviscerated horses.

The condition in this case suggests that there may be some justification for the opinion of Beau and Massiat.

PART III.

We have to thank Dr. Risien Russell for the opportunity of observing the following experiments upon animals performed by him at the suggestion of one of us (J. H. J.) for the elucidation of this subject:—

Experiment I. Female Macacus rhesus. Ether anæsthesia.—In the earliest stage of the anæsthesia the respiratory movements were quiet and chiefly abdominal. There was a distinct elevation-expansion movement of the whole chest during inspiration, and there was marked eversion of the lower ribs during inspiration. With deeper anæsthesia, but before the corneal reflex was lost, the abdominal respiratory movements became much exaggerated. (Dr. Russell informs us that this is the rule in the lower animals.) At this stage the chest, with the exception of the lowest ribs, sank during inspiration. The supra-clavicular regions and the upper intercostal spaces were "sucked in" during inspiration. This sinking of the chest was certainly due, as Dr. Russell suggested, to the aspiratory effect of the strongly acting diaphragm upon the comparatively soft ribs of the monkey, and this aspiratory effect entirely masked any elevation-expansion movement. The stage of anæsthesia at which this occurred was an early one, and at the corresponding stage of ether anæsthesia in the human subject no thoracic paralysis is met with. When complete anæsthesia was reached diaphragmatic movement became quiet and regular, the chest sank quietly during inspiration; there was, indeed, no trace of any elevation-expansion during inspiration, but the lower ribs were markedly everted.

In order to exclude the possibility of any obstruction in the larynx producing the peculiar respiratory movements mentioned, the trachea was divided and a canula was introduced. The abnormal respiratory movements remained unaltered.

The anæsthesia was then allowed to pass off until the elevation-expansion movement of the chest during inspiration returned. More ether was once more administered; on the deeper anæsthesia produced the same sequence of events as occurred on the first etherisation was again observed; first of all, exaggerated diaphragmatic action with passive "sucking down" of the upper chest during inspiration; and next, quiet diaphragmatic action with eversion of the lower ribs and gentle sinking of the thorax during inspiration.

The ether anæsthesia was again allowed to pass off, when the elevation-expansion movement of the chest during inspiration returned. Chloroform was then administered, and the same effect was observed as with ether, but it was much more rapid. During deep anæsthesia the trachea was clamped, and a few inspiratory movements preceded death.

Experiment II. Dog. Ether anæsthesia.—During the earliest stage of the anæsthesia the elevation-expansion movement of the thorax in inspiration became exaggerated. During the next stage—that in which there is rigidity, this movement was little marked owing perhaps to the rigidity of the trunk muscles (abdominal, thoracic and spinal muscles). With deeper anæsthesia when the rigidity had disappeared the thoracic elevation-expansion movement in inspiration again became exaggerated. With still deeper anæsthesia the thoracic expansion during inspiration ceased, and was replaced by sinking of the chest during inspiration; the movements of the chest and the abdomen alternating. The diaphragm was acting well, and the lower five ribs were markedly everted by the diaphragm.

Tracheotomy was now performed. The anæsthesia was allowed to diminish and ether was later again administered. The same sequence of events occurred as upon the etherisation before tracheotomy.

When in the stage of deep anæsthesia, the intercostal movements were lost, and whilst the chest and the abdomen were moving alternately, the paralysis of the intercostals quickly gave place to marked intercostal action if the anæsthetic were discontinued for a short time.

The intercostal muscles were now exposed on one side and their condition observed both in slight and in deep degrees of anæsthesia. Under the first condition they could be seen and felt to be in vigorous action and in the second condition not to be acting at all.

The abdomen was then opened by a medium longitudinal incision from sternum to pubes, and the intestines were drawn out so as to do away with abdominal pressure. In this condition the anæsthesia was increased until there was complete loss of the elevation-expansion movement of the chest during inspiration, the abdominal and thoracic movements alternating, and yet notwithstanding the fact that all support had been removed from the abdominal surface of the diaphragm, the eversion of the lower ribs was as marked as before the abdomen was opened.

The effects of the chloroform were then observed, and were similar to, but more rapid than those of ether.

A CONTRIBUTION TO THE STUDY OF THE PYRAMIDAL TRACT IN THE CENTRAL NERVOUS SYSTEM OF MAN.

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From the William Pepper Laboratory of Clinical Medicine.

(THE PHŒBE A. HEARST FOUNDATION.)

IN the March, 1898, number of the *Journal of Nervous and Mental Disease*, Dr. H. A. Hare published a case of unusual œdema in hemiplegia. The brain from this patient was given to me by Dr. Hare and Dr. Harris, the pathologist who performed the necropsy. I was unfortunately unable to obtain the spinal cord, and the tract that I am about to describe could not be followed, therefore, below the lower part of the medulla oblongata.

I examined carefully the brain, and in a horizontal section made at the level of the superior part of the optic thalamus and caudate nucleus I found a recent hemorrhage in the external capsule and lenticular nucleus of the left side. This hemorrhage appeared to be about the size of a hickory nut, and the brain substance around it was softened, more especially on the inner side of the focus. The anterior part of the posterior limb of the internal capsule was evidently involved in the softening, but the optic radiations, except perhaps in their most superior part, appeared, macroscopically, to be intact. In a section made horizontally through the left hemisphere, one inch below and parallel to the first section, no evidences of any lesion were seen.

The case was a very suitable one for the Marchi method, as the patient had lived sufficiently long after the development of the hemiplegia for secondary degeneration to be well advanced.

I noticed in sections stained with osmic acid (Marchi's method) from the lower part of the medulla oblongata, a group of degenerated fibres lateral to the anterior horn. In tracing the tract towards its origin I used the greatest care to avoid mistake. The segments to be placed in Marchi's fluid of course had to be very thin, and to avoid the loss of a segment at any part where the tract might make a sudden bend, and, therefore, render the following of it difficult or impossible, I cut with the microtome each segment entirely before I took another piece from the medulla oblongata. In this way I knew the position of the tract in the segments as they were successively studied, and was able to trace the tract to its separation from the degenerated pyramidal fibres; and at a point where it did make an abrupt bend I could follow it without any danger of error. It is not altogether easy to trace an unknown bundle throughout its course by the Marchi method, for the loss of a small segment may lead to confusion.

A brief description of my findings was published in a discussion of a paper by Dr. E. L. Mellus, read before the Philadelphia Neurological Society.[1]

The origin of the tract could not be determined. Its fibres were mingled with those of the degenerated pyramidal fibres arising in the left hemisphere, and as the lesion that caused the degeneration was on a level with the upper part of the optic thalamus, the tract in question must have arisen as high as the situation of this lesion. It may have arisen in the lenticular nucleus, or thalamus, or it may have come from the cortex. Very slightly below the level of the exit of the fifth nerve from the pons, a band of fibres could be seen distinctly separating from the outermost and lateral portion of the left pyramidal tract. This separation was at first gradual, and the two bundles remained close together for a short distance. Lower in the pons the more dorsolateral of these two tracts passed quite abruptly backward

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[1] SPILLER. *Journal of Nervous and Mental Disease*, March, 1899, p. 178.

and slightly laterally, and entered the trapezoid body. At this portion of its course, in a transverse section, the bundle in passing backward formed a long and narrow band of horizontal lines of black dots, showing that the fibres were cut longitudinally. At the junction of the medulla oblongata and the pons it took a position lateral to the uppermost portion of the inferior olive. As the inferior olive increased in size, the bundle passed backward, and where the olive had its greatest width the bundle was on the posterior and lateral side of the lower olive, at the periphery of the medulla oblongata. The bundle remained on the left side below the motor decussation, but it could not be followed below the level of the first cervical segment, as the spinal cord could not be examined. The degenerated fibres forming this tract were numerous. In the medulla oblongata the position of the tract was very similar to that of Gowers' bundle.

Gowers' tract has been studied by many investigators, but Hoche says that his two cases (1896) were the first in which the tract in adult man could be traced to its termination in the cerebellum. Patrick traced it as far as the corpora quadrigemina.

According to Hoche, the extent of Gowers' tract, as shown by secondary degeneration, depends very much on the location of the lesion producing this degeneration. When the lesion is situated low in the cord the degeneration does not extend above the cervical region. The method of staining also makes a very great difference, as the fibres in the upper part of the tract are so scattered in places that the loss of these fibres is not detected by the Weigert hematoxylin stain.

Hoche refers to the fact that Gowers could not trace the tract above the upper part of the cervical swelling, and the lesion in his (Gowers') case was in the upper portion of the lumbar swelling; and that Schaffer could not trace it by the Marchi method above the second cervical root. If further investigations confirm these observations, Hoche thinks it is probable that only the fibres of Gowers' tract from the upper and middle thirds of the spinal cord are in relation with the cerebellum, and that those from the lower third of the cord connect cells within the cord at lower and higher levels, *i.e.*, those within the lumbar and sacral region with those within the cervical. If this view is correct it seems reasonable to suppose that descending fibres may be contained within Gowers' tract.

The course of Gowers' tract as described by Hoche is very different from that of the tract seen by me. In the first place, Hoche was describing ascending degeneration, from a lesion in the seventh thoracic segment in his first case, and I have observed descending degeneration. At the motor decussation the position of Gowers' tract as given by Hoche (fig. 3, case 1) corresponds with the position of my bundle. The position of the tract in figs. 5 and 6 is also similar to that of my bundle, but in fig. 7 (the level of the knee of the facial nerve) the resemblance ceases. From here on Gowers' tract, as described by Hoche, passes dorsally, and my tract passes ventrally.

Hoche could not trace Gowers' tract beyond the posterior corpora quadrigemina in either of his two cases, and he found that the tract turned upon itself and entered the cerebellum in such a way that in sections taken from the upper part of its course the tract was obtained at two different parts in the same section. The fibres of Gowers' tract entered the cerebellum partly in the velum medullare anticum, partly in the anterior cerebellar peduncle.

Below the primary lesion of the spinal cord in Hoche's first case, degenerated fibres were found in Gowers' column as far as within the lumbar region, but this does not prove that Gowers' tract degenerates downward.

The results obtained by Rossolimo in man are very different from those of Hoche.[1] Rossolimo[2] believed that Gowers' tract terminates in the posterior corpora quadrigemina, the substantia nigra and the globus pallidus. Quensel's[3] paper is in support of Hoche's findings in great part.

Figures 1, 2, 3, 4 and 5 in Bruce's[4] article show that the ventral cerebellar tract occupies a position similar to that of

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[1] HOCHE. *Archiv fur Psychiatrie*, vol. xxviii., 1896, p. 510.
[2] ROSSOLIMO. *Neurologisches Centralblatt*, 1898, p. 935.
[3] QUENSEL. *Neurologisches Centralblatt*, 1898, p. 482.
[4] BRUCE. BRAIN, vol. xxi., p. 374

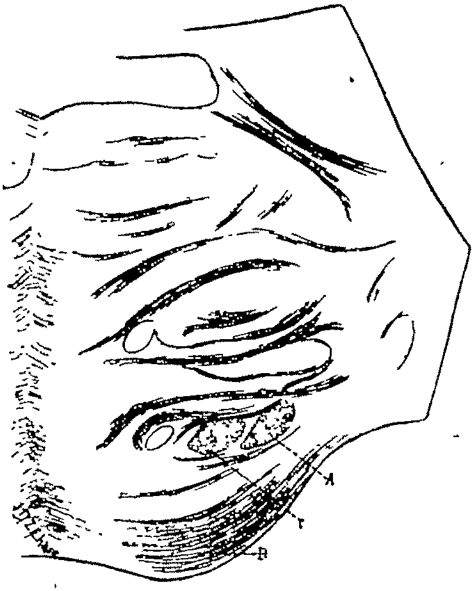

FIG. 6.

The degenerated bundle A has become separated from the adjoining fibres of the pyramidal tract in C. B, fibres of middle cerebellar peduncle. Fig. 6 represents the position of the bundle seen in fig. 1.

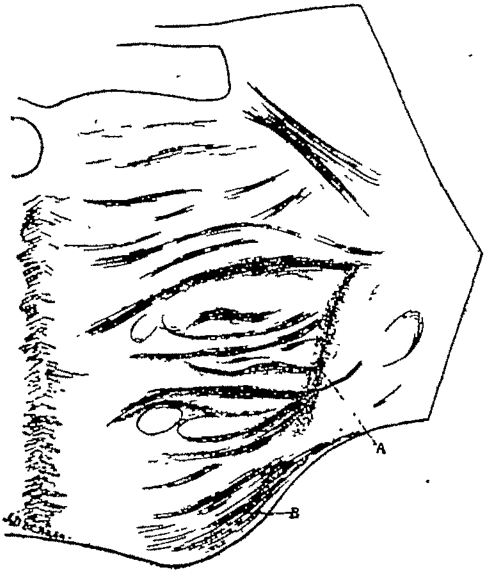

FIG. 7.

The bundle A is seen in longitudinal section. Fig. 7 represents the position of the bundle seen in fig. 2.

my bundle in the medulla oblongata, but in the pons the two tracts separate very widely.

In speaking of the afferent ventro-lateral tract, Russell[1] says that the position of this tract in the fifth and all other

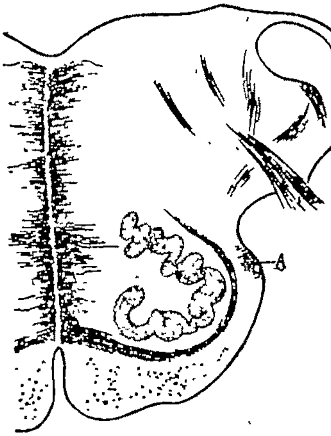

FIG. 8.

Fig. 8 shows the relation of the bundle A to the lower olive.

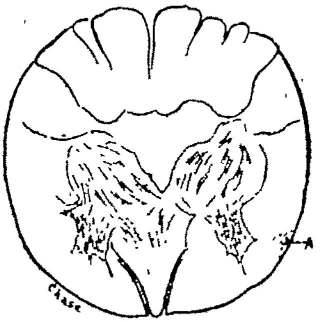

FIG. 9.

Fig. 9 shows the bundle A at the lower part of the motor decussation. Fig. 9 represents the position of the bundle seen in fig. 4.

segments of the cervical cord on the cephalic side of the lesion was more or less midway between the periphery of the cord and gray matter of the ventral horn, the band of fibres between this sclerosed area and the periphery of the cord being absolutely intact. This statement differs from those of most authors. My band of fibres in the upper cervical region is exactly on the periphery of the cord and this would seem to be a further proof that it is not a part of Gowers' tract.

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[1] RUSSELL. BRAIN, vol. xxi., p. 170.

Campbell,[1] in his excellent digest on the tracts of the spinal cord, says Gowers' tract degenerates in an ascending direction, and he makes no reference to a descending degeneration of this tract. V. Bechterew thinks it is probable that in some cases in which a descending degeneration of Gowers' tract has been observed, the degeneration was really in Loewenthal's anterior marginal bundle, although v. Bechterew[2] does not entirely exclude the possibility of descending fibres in the fasciculus antero-lateralis.

There seems to be considerable doubt as to whether Gowers' bundle does degenerate downward, and as far as I know no case has yet been reported in which this tract was degenerated in man as the result of a cerebral lesion.

I find an interesting statement authorised by Schäfer[3] in "Quain's Anatomy." It is said that in the monkey a few fibres of the antero-lateral column degenerate after lesions of the cerebral hemisphere of the opposite side. "They are mingled with those of the descending cerebellar tract and with those of the tract of Gowers, and are connected with cells in the Rolandic region of the cerebral cortex, as shown by the fact that they degenerate after lesions of that region. These fibres may perhaps be regarded as belonging to the system of the direct pyramidal tract, which in the monkey does not exist as a well-marked tract as in man: it has not yet been ascertained whether they occur in man as well as the direct pyramidal." These fibres are said to degenerate after a lesion of the *opposite* cerebral hemisphere.

Loewenthal[4] described two bundles in the lateral column

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[1] CAMPBELL. BRAIN, vol. xx., p. 522.

[2] v. BECHTEREW. *Die Leitungsbahnen im Gehirn und Rückenmark*, second edition, pp. 82, 90.

[3] "Quain's Elements of Anatomy," vol. iii., part I., p. 25.

[4] LOEWENTHAL. *Revue Médicale de la Suisse Romande*, 1886, p. 529.

of the cord in the cat and dog; one situated in the dorsal segment of the lateral column he called the intermediate system of the lateral column (système intermédiaire du cordon latéral); the other, situated in the ventral segment of the antero-lateral column he called the anterior marginal bundle (faisceau marginal antérieur). He did not know the origin or termination of these tracts. This anterior marginal bundle might be thought to be the same as my tract, but recent investigations seem to indicate that Loewenthal's bundle comes from the cerebellum.

My tract could hardly be confounded with the intermediary system of Loewenthal. The major part of it does not occupy the mesial portion of the antero-lateral column in front of the lateral pyramidal tract. The literature on this tract is given by Campbell (*l.c.*) and v. Bechterew (*l.c.*).

The fibres in the peripheral part of the ground bundle of the antero-lateral column that degenerate downward, according to v. Bechterew, are the spinal portion of the posterior longitudinal bundle and the fibres from Meynert's decussation that arise in the anterior corpora quadrigemina; the fibres of Forel's decussation that arise in the lateral portion of the thalamus and the nucleus ruber; the vorderes Randbündel that arises in the cerebellum; and finally the olivary tract, coming from the lower olive (*l.c.*, p. 80).

By vorderes Randbündel, v. Bechterew means Loewenthal's faisceau marginal antérieur. From the investigations of Marchi, Biedl, and Basilewski (the latter in v. Bechterew's laboratory) v. Bechterew concludes that this tract arises in the cerebellum.

The tract described by v. Bechterew,[1] Held,[2] and Boyce,[3] as arising in the anterior corpora quadrigemina, certainly could not be confused with my tract, and its location within the spinal cord is entirely different from that of the fibres observed by me. The tract arising in the thalamus is also very different (Boyce, v. Bechterew).

Risien Russell, in experimenting on dogs and monkeys, cut the lateral portion of the medulla oblongata between the "ascending" root of the fifth nerve and the inferior olive, and observed descending degeneration in the antero-lateral column. He regarded this tract as the same as that described by Boyce. This tract observed by Risien Russell differs somewhat from the one seen by me. I can only compare the cervical region in each case, as I was unable to trace my tract below this region and Russell did not trace his above, on account of the location of the primary lesion. The fibres in my case occupied a very small portion of the area represented as degenerated in Russell's figure 2, and if Russell's tract was identical with that described by Boyce, as Russell believed, then its origin was very different from the origin of my tract. None of the degenerated fibres in my case were situated just ventrally to the crossed pyramidal tract and internally to the anterior part of the direct ascending cerebellar tract, as Russell[1] described in his case.

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[1] v. Bechterew. *Neurologisches Centralblatt*, 1897, p. 1074.

[2] Held. *Archiv f. Anatomie u. Physiologie. Anatom. Abth.*, 1893, p. 289

[3] Boyce. *Neurologisches Centralblatt*, 1894, p. 466.

My tract cannot be confused with that described by Marchi, Biedl,[2] and Thomas,[3] as arising in the cerebellum; although its position may be similar, its origin distinguishes it at once. It cannot be confused with the tract resulting from injury of Deiters' nucleus and other structures in the lateral region of the medulla oblongata (Ferrier and Turner,[4] Risien Russell[5]) for the same reason; or with the fibres seen by Mott.[6]

Risien Russell has described a tract situated not very far from the position of my bundle. The case was one of tumour of the cerebrum. In addition to the degenerated pyramidal fibres studied by the Marchi method, he found another and quite distinct tract of degeneration seen on the side of the lesion, and occupying the ventral margin of the medulla, just outside and opposite to the ventro-external angle of the inferior olive. It was a well-defined band of degeneration, quite distinct and separate from the degenerated pyramid, lying between the external arcuate fibres as they course round the medulla opposite the inferior olive. Russell[1] was unable to establish a connection of this tract with any of the degenerated fibres met with in the pons. A little lower in the medulla oblongata this tract was found in the lateral region opposite the ventral tip of the anterior horn. He believed that this tract was not derived from the degenerated pyramid.

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[1] RUSSELL. BRAIN, vol. xx., p. 409.

[2] BIEDL. *Neurologisches Cetralblatt*, 1895, p. 434.

[3] THOMAS. *Le Cervelet.*

[4] FERRIER and TURNER. *Phil. Trans. Royal Soc.*, 1894, vol. clxxxv., B.

[5] RUSSELL. BRAIN, vol. xx.

[6] MOTT. BRAIN, 1895.

This tract observed by Russell does not seem to be the same as the one observed by me. Russell was unable to satisfy himself as to the precise point of origin of his fibres. The position of the tract was not that occupied by the degenerated fibres in my case. It was at the periphery of the medulla oblongata and opposite the ventro-external angle of the inferior olive. My tract was also at the periphery but dorso-external to the inferior olive, and at some distance from the place occupied by Russell's fibres. In the cervical region Russell's tract seems to have occupied a more anterior position than mine.

In Thomas'[2] recent review of certain descending tracts in the antero-lateral column I do not find the description of any tract exactly similar to mine.

I believe that the tract described in this paper has hitherto been unrecorded. If I am in error in this I shall cheerfully accept correction. One case may not be sufficient to establish the existence of an unknown tract, and should confirmation of my findings not be granted, I may have to assume that the bundle of fibres seen by me was an aberrant bundle from the pyramidal tract, and not usually present in the central nervous system. This explanation does not seem probable, but I mention it in order to be as guarded as possible in all statements relating to scientific matters.

There are a few more tracts described by others that might be mentioned in this connection, but the resemblance to my bundle is not very great; such, for example, as the tract coming from the lateral fillet observed by Ferrier and Turner,[1] or v. Monakow's[2] "aberrirendes Seitenstrangbündel" or Pick's bundle, which has been found by Hoche[3] to degenerate downward.

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[1] RUSSELL. BRAIN, vol. xxi., p. 145.

[2] THOMAS. *Journal de Physiologie et de Pathologie Générale*, No. 1, 1899.

The existence of homolateral fibres in the crossed pyramidal tract on the side of the cerebral lesion has been noted by a number of observers. The origin of these fibres in the degenerated pyramid of the same side seems to have been first observed in 1894 in a cat by Russell.[4] The limited literature on the subject is given by him. I may add a reference to the paper by Dejerine and Long,[5] and one to the paper by Redlich.[6] In my preparations the origin of these homolateral fibres in the degenerated pyramid was distinct.

Dejerine and Long (*l.c.*) in cases of hemiplegia, studied by the Marchi method, observed degenerated fibres that left the anterior pyramid, took a horizontal course, mingled with the external anterior arciform fibres, passed in front of the arcuate nucleus, and decussated in the median raphe. These fibres were not traced beyond the interolivary layer of the opposite side. Similar fibres are also described by Redlich (*l.c.*) in experimental work.

The brain from a case of cerebral tumour was given to me by Dr. C. W. Burr. It was studied by the Marchi method. In addition to the usual degeneration of the pyramidal tract, I found degeneration of the postero-external columns, of equal intensity on the two sides, and the degeneration of the external anterior arciform fibres, described by Dejerine and Long, was very distinct. I was unable to follow these fibres beyond the interolivary layer of the opposite side.

I am indebted to Drs. C. Y. White and S. S. Kneass, associates in the Pepper Laboratory, for the photographs, and to Mrs. P. P. Chase for the drawings.

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[1] FERRIER AND TURNER. *Phil. Trans. Roy. Soc.*, 1894, vol. clxxxv. B.

[2] v. MONAKOW. *Archiv f. Psychiatrie*, vols. xiv. and xxii.

[3] HOCHE. *Archiv für Psychiatrie*, vol. xxx., 1898.

[4] RUSSELL. BRAIN, vol. xxi., p. 145.

[5] DEJERINE AND LONG. *Comptes rendus de la Soc. de Biologie*, 1898, p. 864.

[6] REDLICH. *Neurologisches Centralblatt*, 1897.

DESCRIPTION OF FIGURES.

FIG. 1.

The bundle A is separated as a distinct band of degenerated fibres, and is seen in transverse section; at a little higher level it is united with the portion of the pyramidal tract designated by D. Fibres of the middle cerebellar peduncle are seen on the extreme right of the photograph.

FIG. 2.

The bundle A is seen in longitudinal section, with a low-power lens. It begins at this level to pass posteriorly. By mistake it is represented on the right side of the pons instead of on the left. Fibres of the middle cerebellar peduncle are seen at the lower left corner of the photograph.

FIG. 3.

(Same as fig. 2.) The bundle A is seen under higher magnification, and the degree of degeneration, as indicated by Marchi's method, is shown.

FIG. 4.

The bundle A is shown under low-power at the periphery of the cord, extending about as far forwards as the anterior end of the anterior horn (E). The anterior horn is seen on the left of the photograph. The bundle A is, by mistake, represented on the right side of the cord instead of on the left.

FIG. 5.

(Same as fig. 4.) The bundle A, which is somewhat indistinct in fig. 4, on account of the low-power lens employed, is seen in this photograph under higher magnification.

Figures 6, 7, 8, and 9 are diagrams showing the relative position of the bundle A.

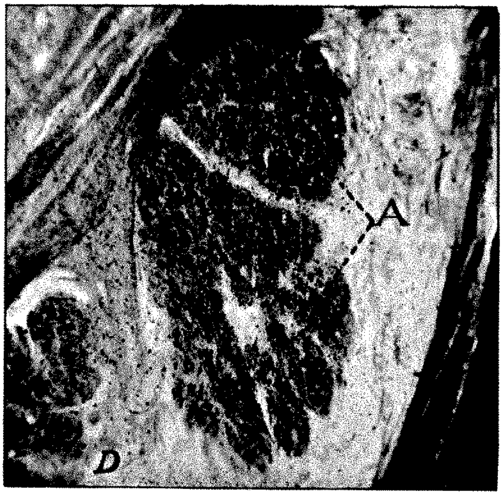

FIG. 1.

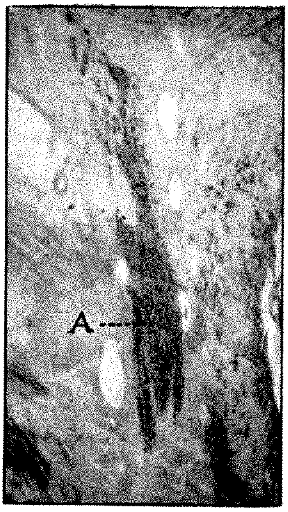

FIG. 2.

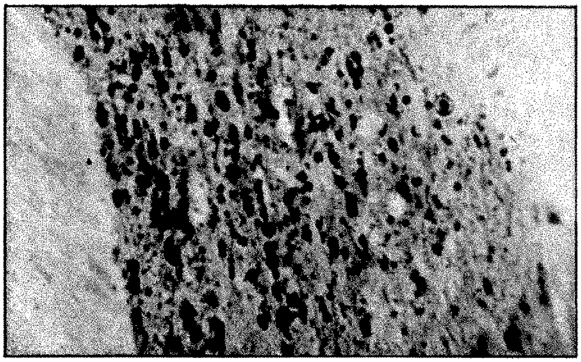

FIG. 3.

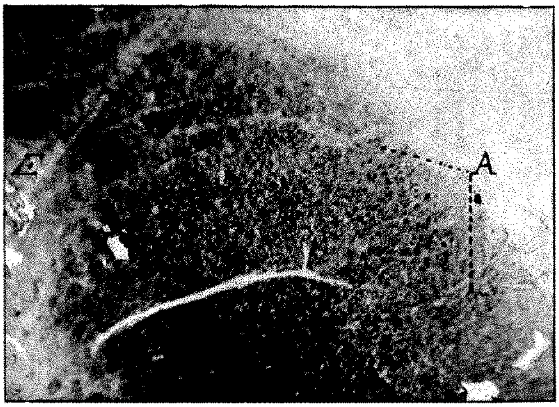

FIG. 4.

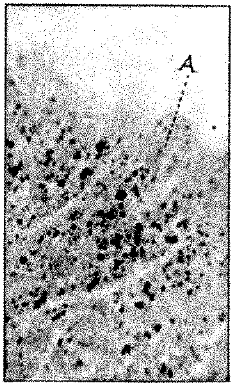

FIG. 5.

NOTE ON A FORM OF DEMENTIA ASSOCIATED WITH A DEFINITE CHANGE IN THE APPEARANCE OF THE PYRAMIDAL AND GIANT-CELLS OF THE BRAIN.

BY JOHN TURNER, M.B.ABER.

I WISH to draw attention to certain cases of mental disease which present a definite pathological anatomy and of which I have not been able to find any previous description.

The lesion shows itself chiefly in the nerve-cells and appears to be of widespread distribution, attacking the great majority of the pyramidal nerve-cells in all parts of the cerebral cortex (frontal, ascending-frontal, occipital being the regions examined).

It is especially well marked in the giant nerve-cells of the ascending convolutions, and for this reason I have chosen cells from this part for my description and photographs.

It is not a common change in insanity, as in considerably over a hundred brains of lunatics examined by Nissl's method or modifications I have besides the cases here noted only seen one or two individual cells so affected.

In the case of a man whose leg had been long amputated, no cells of this description were found in the opposite leg centre of the cortex.

The lesion appears to be identical with that described by Nissl and others after section of the axon of a motor nerve-cell, and by Barker in the forehorn-cells in cases of epidemic cerebro-spinal meningitis (see *British Medical Journal*, December 26, 1897); but it is questionable how far this similarity extends; at any rate, with osmic acid, very definite alterations of structure are shown both in nerve-cell and its axis-cylinder continuation, which point to a probably degenerating state of the neuron. Although in one of the seven cases there was no mention made of a condition of dementia, but only prolonged and profound melancholia, I am inclined to think that the lesion is the anatomical groundwork of the dementia, which is often rapid in its course and probably always fatal.

Cases Nos. 1 and 2 are of interest, as with a clinical history resembling to a certain extent general paralysis in its acuter forms, the autopsy revealed naked-eye appearances quite distinct from general paralysis, neither did the microscopical investigation show any features in common with this latter disease.

As regards the melancholia case (No. 5), it is to be noted that she contracted a malignant form of diphtheria affecting the whole of her œsophagus and to which she succumbed after an illness of a fortnight.

In case No. 4 I was able from the symptoms to foresee the nature of the changes in the nerve-cells.

Certain symptoms were present in most of the cases, and of these the most obvious was paresis. The patient, for no obvious reason, occasionally fell down whilst walking, and ultimately there was complete inability to walk. Possibly the weakness of the arms was as great, but was not so obviously developed.

When the notes of the cases do not mention incapability of walking, there is mention of involuntary jerkings of the limbs. The demented condition of the patient prevented any greater precision in testing their movements, and the same cause interfered largely in endeavouring to determine sensory defects. The sensibility to pricking (painful impressions), in the cases where any reliance could be placed on the results, was greatly blunted, or entirely absent, but generally more marked in the lower extremities.

The pupils reacted to light and for accommodation to the end. The knee-jerks were exaggerated; plantar reflexes absent; tongue free from tremor; articulation not generally interfered with.

The arterial tension of three cases was high (= 150 to 210 mm. Hg.). This is interesting in view of the fact that a thickening of the arterioles of the cortex and minute cerebral hæmorrhages were found in all the cases.

Diarrhœa was very commonly noted towards the end.

The whole case may run a fairly rapid course, varying from a few to eighteen months, or, after prolonged mental disorder (melancholia so far only noted), dementia sets in and death as a rule rapidly ensues.

PATHOLOGICAL ANATOMY.

A reference to the cases will show the leading naked-eye changes noted in the head and viscera. The brain may present a fairly healthy appearance, or there may be merely evidence of atrophy in the frontal convolutions. In others the meninges are opaque and thick over the vertex, but not adherent, and, microscopically, this thickening is seen to be an increase in the connective tissue of the arachnoid, and quite unattended with any round-cell infiltration of the pia.

A general feature noted microscopically in all the sections examined was a thickening of the arterioles and capillaries of the cortex. Sometimes the lumen was nearly obliterated. In the arterioles this thickening appears to be due to increase of the muscularis and adventitia; in the capillaries, to a fibroid thickening. Probably, in both cases, this latter predominates, for when stained in picro-fuchsin, the thickened vessels stand out as prominent red rings or lines. Tortuosity was also noted to a very considerable extent. Minute hæmorrhages into the cortex (microscopical) were seen in all the cases, sometimes five or six in one section.

The larger vessels of the white matter often had a copious collection of colloid bodies lying in their immediate neighbourhood. They showed a blue centre fading into a red circumference when stained with acid fuchsin and toluidin blue.

There was never any appearance of spider-cells or proliferation of neuroglial fibrils.

Nerve cells.—As noted before, the change in these is widespread, and appears to affect the majority of all the pyramidal cells, and is especially well seen in the giant-cells.

Fresh squeezed-out portions of cortex, coloured in methylin blue or toluidin blue, show the change with the greatest clearness, and my experience, contrary to that of Drs. Robertson and Orr, is that most pathological changes are better seen by this method, when properly carried out, than in sections.

The cell is probably smaller than in its normal state, except when distended with pigment, and often somewhat globular; it has generally an irregular border staining deeply, and which often fails to show definite chromophile elements. The whole centre of the cell consists of a pale, homogeneous mass, having a blurred or washed-out appearance.

The nucleus, which is small and shrunken, stains a pale blue, and is situated at the periphery of the cell, or it may be up in its apex, or in the junction of a dendrite with the cell. It contains a dark, round or oval, and probably shrunken, nucleolus.

Generally a large part of the cell is occupied by a highly refractive bright yellow pigment, and this may distend the cell enormously in one direction. This substance stains either a dark brown or jet black with osmic acid,[1] but that it is not wholly of a fatty nature is rendered probable by the fact that it is still seen in the cells in sections which have been subjected to chloroform and xylol. Generally a fair number of dendrites are given off from the cell, but they are, as a rule, unduly thin, and stain of a pale uniform blue, or else show a few attenuated chromophile threads.

The apex, at its junction with the cell-body, generally shows a few fine chromophile threads, but further along it does not stain at all, and is barely visible. Very often there is an abrupt line of demarcation separating the pale apex from the densely-stained cell-body border (see fig. 1).

In sections, fixed in sublimate and stained in toluidin blue, the appearance of the cell-body is much the same as in films; the pigment appears of a greenish colour, owing, probably, to the blending of its yellow with the blue stain. The nucleus is almost always shrunken, and, with a distorted outline, contains only a few loose granules and a dark nucleolus, and is almost always eccentrically placed—often, indeed, bulging from the cell-body. The pale, almost colourless, hyaline-looking body of the cell, which generally has a somewhat circular contour, gives these cells a most characteristic appearance; the pigment is often almost imperceptibly blended with it at its outer part. Even with a one-twelfth oil immersion, it appears homogeneous. In other respects, the description given of the whole cells applies to those seen in optical section.

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[1] This refers to cells which have been hardened in osmic acid; in the case of films the pigment merely becomes slightly darker and takes on a dull greenish tint.

Case No. 6, which was examined after fixing in osmic acid,[1] gave very interesting results.

The tangential fibres of the first layer were present in fairly large numbers, and showed a normal appearance in the motor region, but in the frontal regions they were practically absent.

In the motor region the great majority of the medullated nerve-fibres in the lower strata of the cortex and the adjacent white matter showed very marked changes; the staining, in general, was not so dark, owing to the fact of disappearance of some of the myelin, and that which remained was in the form of little separate black drops on either side of the nerve-fibre, which could be seen in its place more darkly stained than usual; and often in advanced cases of degeneration, when no myeline remained, it was nearly black. Fig. 4 shows a degenerated medullated fibre.

In certain parts of the section medullated nerve-fibres were seen, which gave a normal reaction with osmic acid, and some of these are shown in fig. 4, to contrast with the former figure.

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[1] I find that a mixture of carbolic acid, 5 per cent., osmic acid 2 per cent., in equal parts, gives excellent results; it penetrates with great rapidity, fixes the smallest particles of degenerated myelin or fat, and also preserves the nerve-cells well. The pieces are left in it for twelve to twenty-four hours, then placed in 10 per cent. formaline for two days, passed into alcohol for one or two days, and then through chloroform and into paraffin. The section is fixed to the slide by capillarity, and then decolourised in permanganate of potash, followed by sulphurous acid. These sections counterstain very well with Ehrlich's acid hæmatoxylin, which is only allowed to act for a second on the section, and then washed off.

SYNOPSIS OF CASES.

No. 1.—I. B., a female, admitted June 29, 1898, aged 45, married. Her father was a drunkard and died about 50 of apoplexy. Her mother is stated to have had several "fits," in one of which she died. Mother's sister melancholic. This is her first attack, of eighteen months' duration, and stated to be due to menopause and alcohol; it began with depression and occasional violent fits. She has been addicted to alcohol for years.

The facts certifying to her insanity were incoherent shouting and raving. On admission she was in feeble condition and weighed only 88 lbs. Temperature normal; complexion turgid; knee-jerks exaggerated; pulse (sitting), 158. Has conjunctivitis. Was restless and noisy; obstinate, paying no heed to questions. Dirty in habits; bad appetite. Parotitis of right side developed five days after admission. Teeth covered with sordes and mouth full of muco-purulent slime. Was in a delirious state, muttering, but occasionally replying relevantly. Her speech thick and indistinct. Plantar reflexes abolished. Was very restless, occasionally screaming, and had frequent attacks of involuntary jerking of the limbs. Became worse; comatose. Left pupil the larger, they both react slightly to light. Face covered with a greasy sweat; mouth open; eyes closed. On July 7 she died. Autopsy seventeen hours later. Body fairly nourished. Blood vessels at base normal. Meninges fairly clear and stript readily; they were heavily waterlogged over the anterior two-thirds. Lateral ventricles dilated and filled with blood-tinted serum. Atrophy of convolutions of anterior two-thirds. Consistency of brain was normal. No granulations in any of the ventricles. Pons and cerebellum appeared normal. Small patch of consolidation in left lung; old adhesions of right side. The cardiac muscle was rather soft; valves normal. Liver congested; spleen firm; kidneys slightly granular.

Weights in grammes.—Cerebrum (stript), 988; meninges, 20; cerebellum, 133; stem, 27; total, 1,168. Heart, 208; liver, 1,208; spleen, 128; right kidney, 143; left kidney, 165.

The idea was present that this was an acute case of general paralysis, but the entire absence of any of the pathological appearances, macroscopical and microscopical, showed conclusively that it was not.

No. 2.—J. W., a female, admitted October 15, 1897, widow.

This is her first attack, and is said to be of only ten weeks duration, following influenza. Has been a hard-working, sober woman. Aged 52.

The facts certifying to her insanity were: irrational conversation; at times morose, and says she is a lost woman; at others hilarious, laughing and singing immoderately. On admission she is thin, and weighs 93 lbs. Temperature normal. Dark sallow complexion, coarse skin. Pupils equal, and react normally to light and on accommodation. Knee-jerks exaggerated. Tongue free from tremor, furred. Slight cough. Nocturnal urine, acid, 1016; no albumen. Is excited, spits on the floor, and answers rudely when remonstrated with; sings when her chest is being examined; replies in a flippant, careless way, "don't know," to most questions. In December it is noted that, as a rule, she is excited one day and quiet the next. The left pupil is slightly the larger; they both react well to light and on accommodation.

March 24, 1898.—The day before yesterday she fell forwards on her face whilst walking round the farm; was not convulsed, and did not lose consciousness. This has happened several times recently. Is now in bed, talking to herself. Tongue clean, pulse 75, arterial tension = 150 mm. Hg.

April 2.—Up yesterday, but had to be put to bed again, as she could not stand. Clean in habits. Pulse 78, temperature normal, urine free from albumen, 1010.

April 20.—Up, walks unsteadily, and leans over to the right. Is now very lost and silly.

April 30.—Was yesterday very excited, rushing about the ward and falling about. To-day she keeps chattering a lot of nonsense in a chanting tone. Diarrhœa set in on May 16, and on the 26th she died.

Autopsy (twenty-five and a half hours later).—Poorly nourished. Basal vessels healthy. Meninges not opaque, stript readily, rather thick. No marked wasting of the convolutions; brain of normal consistency. Lateral ventricles dilated. No granulations on them or on fourth ventricle. Both lungs bound down by old adhesions. Heart normal, no atheroma. Liver pale and soft. Spleen firm. Kidneys small, soft, pale; cortex not thin; capsules stript readily.

Weights in grammes.—Cerebrum (stript), 1031; meninges, 20; cerebellum, 120; stem, 27; total, 1,198. Heart, 204; liver, 1,040; spleen, 132; right kidney, 92; left kidney, 76.

No. 3.—E. E. W., female, admitted November 6, 1895, baker's wife. First attack of eighteen years' duration. Her father died of Bright's disease. She has a daughter insane. On admission she weighs 112 lbs., and is in fair health and condition. Knee-jerks exaggerated. Right pupil the larger; they react normally to light and on accommodation. Tongue slightly tremulous, protruded markedly to the right. Urine: specific gravity 1021, a faint trace of albumen. Her mental condition was one of delusional insanity; she imagined that some women were plotting against her and her husband, and conspiring to blow her up with dynamite. She was neat, quiet, and industrious, and gave no trouble, and remained thus till April, 1898, when she made an attempt on her life, and became acutely melancholic, restless, agitated, refusing food, and not able to sleep. Her bodily condition deteriorated greatly, she picked her face, looked miserably ill, and had to be held in bed to prevent her from jumping out and roaming in the ward.

May 17, 1898.—Pulse 102, regular; arterial pressure = 150 Mg. Hg. Knee-jerks exaggerated. Tongue clean. Temperature normal. Is very agitated and looks haggard.

During July she suffered off and on from diarrhœa, and had dermatitis of face and back of hands (probably from the sun). Mentally more composed.

In September she rapidly became demented, dirty in her habits, and very greedy. By November she was bed-ridden, and had lost the use of her legs, was filthy in her habits, very restless, and often falling about.

December 8.—Lies on her right side, and exhibits involuntary jerking movements of arms and legs, and risus sardonicus. The attendant states that she has to be held when seated on the night stool, or she would jerk herself off on to the floor. She died on December 11.

Autopsy (twenty-nine hours later).—Body poorly nourished; rigor mortis present. Skull neither thick or dense: basal vessels healthy. Meninges very thin and transparent, stript readily. Brain very large and pale, with no atrophy or dilatation of lateral ventricles. Lungs small, pale, crepitant; no pleural adhesions. Left side of heart slightly hypertrophied, and mitral orifice small. Slight calcareous deposit at base of aortic valves. No atheroma of aorta beyond. Liver soft and pale. Spleen small and firm. Kidneys small, dark purple colour; cortex tough; capsules slightly adherent.

Weights in grammes.—Cerebrum (stript), 1,132; meninges, 18; cerebellum, 139; stem, 30; total, 1,321. Heart, 215; liver, 885; right kidney, 101; left, 107; spleen, 59.

No. 4.—M. E. B., female, admitted December 20, 1897, aged 37, single. First attack; has always been considered hysterical, but for the last year has been nervous, apprehensive, and could not be induced to leave the house. Gradually lost use of her legs and hands, and the latter shook so much that she could not hold a cup. At times would fall down. Took to her bed several weeks before admission, and a few days ago developed screaming attacks. Said to have been a sober woman.

On admission is ill and unable to walk; slightly bedsore. Temperature, 99·6°. Complexion coarse, skin greasy and blotchy. Knee-jerks absent, plantar reflexes absent, pupils equal. Has bronchitis. Her sensitiveness to pricking is *nil* in face, neck, chest, arms, legs, and there is no local reaction. Is very apprehensive, and shrinks away when one goes near her. Keeps ejaculating little phrases *à propos* of nothing, *e.g.*, "Who speaks English?" "Isn't Mr. Archer?" "For grief I shall read," "*Do* help me." Shouts occasionally. Is dirty in habits. To most questions she pays no heed, but when asked her name replied, "Why, Brass."

Remained in much the same state till she died on December 24, 1897.

Autopsy (three-and-a-half-hours later).—Fairly nourished. Skull heavy and dense; vessels healthy. Meninges congested, but not thick or adherent; they were clear. Some atrophy of the frontal convolutions. Lateral ventricles not dilated. Brain of normal consistency. Evidence of emphysema and bronchitis. Heart muscles soft, apex fatty, valves fairly healthy. Liver soft and dark coloured. Spleen soft. Kidneys fairly healthy.

Weights in grammes.—Cerebrum (stript), 950; meninges, 13; cerebellum, 143; stem, 31; total, 1,137. Heart, 289; liver, 1,629; spleen, 152; right kidney, 145; left kidney, 170.

Sections of the popliteal, post-tibial, radial, and median nerves were examined, after fixing in osmic acid. The peripheral nerves showed very marked changes, some bundles being nearly devoid of all myelin rings (radial and post-tibial). The more central nerves were affected, but to a much less extent.

No. 5.—A. E. C. This woman was first admitted on June 25, 1889, suffering from melancholia, and was discharged, recovered, August 21, 1889, and re-admitted May 13, 1890. Profoundly depressed, restless, and agitated, constantly ejaculating, "Oh, whatever *shall* I do!" in an agonised tone. She remained in this state of deep depression till her death, but up to her last illness she was clean in habits and capable of doing ward work, and never showed any motor troubles. In February, 1898, her arterial tension was 210 mm. Hg. On January 24, 1899, she went to bed with a sore throat, which proved to be diphtheria, and she died February 6 following. Her temperature during this period was always subnormal (taken in the rectum). She was 69 years old.

Autopsy (five hours after death).—She had a thick, ash-grey membrane lining the whole of her œsophagus, but stopping at the cardiac orifice of the stomach; small infarct in spleen. Thoracic viscera fairly healthy. Kidneys granular. Liver soft and dark. Head: basal arteries atheromatous. Large collection of fluid under the meninges, which showed here and there small opaque patches, but were elsewhere thin and translucent, and not adherent. Atrophy of convolutions most marked in parietal regions. No marked dilatation of ventricles.

Weights in grammes.—Cerebrum (stript), 1,084; meninges, 15; cerebellum, 147; stem, 35; total, 1,283. Heart, 238; liver, 1,102; spleen, 129; right kidney, 94; left, 111.

This case is out of harmony with the others, inasmuch as she was not demented in the ordinary sense of the word, and did not exhibit any of the motor troubles seen in all the other cases; but it has to be taken into consideration that she was confined to bed for nearly a fortnight prior to death with a malignant form of diphtheria, and the question arises whether the poison of the diphtheria was the cause of the changes found in the nerve-cells, or whether these changes were associated with her prolonged and profound melancholia.

I cannot help thinking that having regard to the unanimity with which motor disturbances were noted in all the other cases with similarly affected cells, the changes noted in her case were the result in part at least of the diphtheria, although in another case examined shortly before I was unable to discover any notable alteration in the nerve-cells of similar regions.

In the case under discussion, however, the form of disease was asthenic with a persistent low temperature, and in the latter it was rapidly fatal with a considerable pyrexia (104·6).

No. 6.—Male, aged 36. Admitted August 17, 1899. Father insane. First attack of recent origin. The facts certifying to his insanity were incoherence, violence, raving. On admission he weighed 138 lbs., and was in fair condition. Temperature normal. Knee-jerks present. Tongue furred. Pupils equal. He was very restless and incoherent, and paid no heed to questions. Threw himself into peculiar attitudes owing to involuntary jerking of

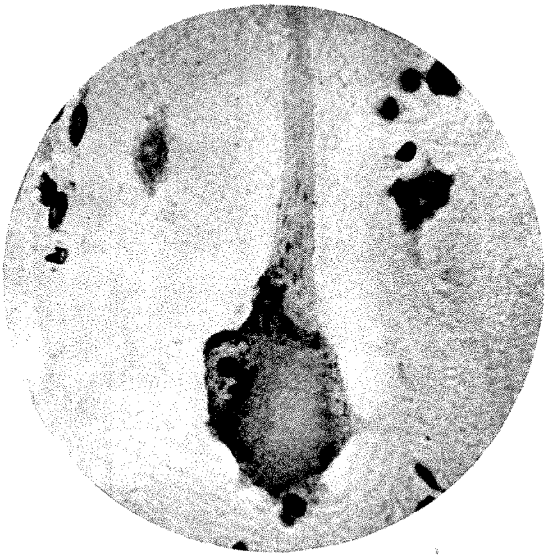

FIG. 1. ($\frac{1}{12}$ oil, No. 2 eye-piece, Beck.)—Cell with nucleus distorted and bulging from the side of cell body. A darkly stained cell body border. Some yellow pigment at right edge. A darkly stained irregular border separates the pale apex from the cell body. In the former are a few very fine short chromophile threads.

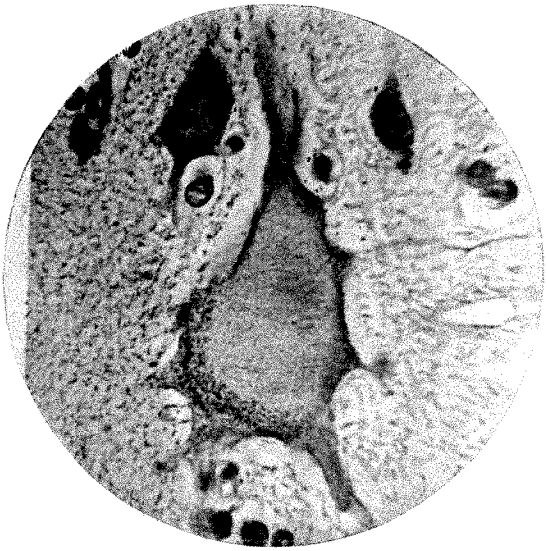

FIG. 2. ($\frac{1}{12}$ oil, No. 2 eye-piece, Beck.)—In this cell the whole of the centre is occupied by a pale washed-out hyaline looking mass. No nucleus is seen, but in serial sections one is seen to be present, situated at the upper right hand side of cell, about where the darker area is shown in the photograph. A mass of rather coarsely grained pigment is seen at the lower left hand border of cell.

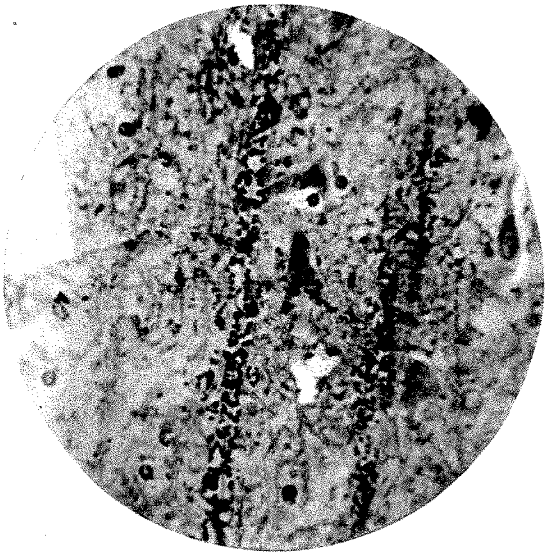

FIG. 3. ($\frac{1}{8}$, No. 2, Beck.)—A degenerated myelin nerve fibre seen in centre of figure, others to the right. The axis-cylinder can be seen in places.

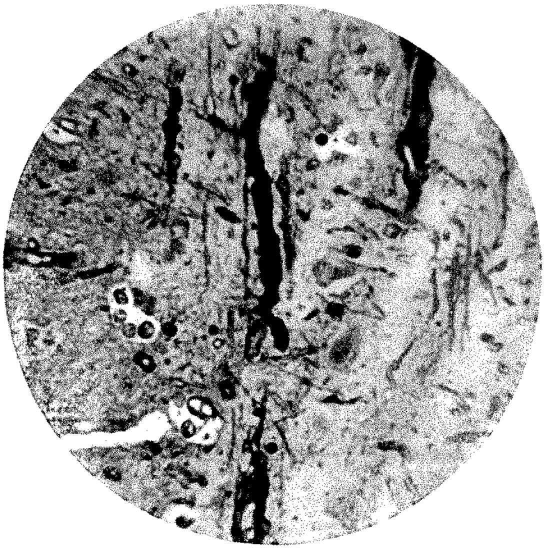

FIG. 4. (Same magnification.)—Normal myelin nerve fibres from other parts of same section.

the limbs, and had to be put in the padded room to prevent him from injuring himself, as he could not stand. Refused food. Rapidly got weaker, but still kept restless and very resistive; laughed causelessly, was dirty in habits. His temperature was subnormal on the two occasions it was taken. Became collapsed on the 21st, and died August 22, 1899.

Autopsy (a few hours later).—Beyond acute congestion of lungs the thoracic and abdominal viscera appeared healthy. Head: skull thick, basal vessels healthy. Meninges very opaque over the vertex, thick, not adherent. Excess of subarachnoidal fluid. Atrophy of convolutions over vertex. Slight dilatation of lateral ventricles. Brain of normal consistency. Cerebellum large. The meninges over the superior worm were opaque and thickened.

Weights in grammes.—Cerebrum (stript), 1,169; meninges, 28; cerebellum, 179; stem, 36; total, 1,412. Heart, 329; liver, 1,650; spleen, 85; right kidney, 111; left, 121.

No. 7.—W. A., male. Admitted July 2, 1892. Aged 52. Father melancholic and committed suicide. This was his first attack. He was acutely melancholic—the picture of misery—and gradually passed from this state into dementia. Picked his hands and head. Paresis of lower limbs was noted about two years after admission. He was bedridden for over a year, and died in March, 1898, of phthisis.

Autopsy (sixteen-and-a-half hours after death).—The lungs showed extensive tubercular changes. There was some atheroma of the aorta. Liver soft and pale. Kidneys pale and tough. Capsules stript well. Head: the basal vessels were atheromatous. The meninges were thick and opaque, but stript readily. Some atrophy of frontal convolutions. Lateral ventricles much dilated. Brain pale and firm. Cerebellum firm.

Weights in grammes.—Cerebrum (stript), 1,084; meninges, 24; cerebellum, 154; stem, 34; total, 1,296. Heart, 214; liver, 1,028; spleen, 109; right kidney, 101; left, 105.

OBSERVATIONS ON THE ASCENDING TRACTS IN THE SPINAL CORD OF THE HUMAN SUBJECT.

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AND
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THIS note deals with the following ascending tracts in the human spinal cord.

(1) Postero-median column.

(2) Dorsal ascending cerebellar tract.

(3) Ventral ascending cerebellar tract, including the nature of the fibres in the ventral lip.

(4) The intra-spinal portion of the fourth posterior cervical root.

The observations were made in two cases which were examined sufficiently early to allow the Marchi method of staining to be used. Such cases are comparatively rare, and more observations are necessary before the course of these tracts can be said to be thoroughly known. We are indebted to Sir William Banks and Mr. Rushton Parker, for permission to record this note.

In the autumn number of BRAIN, 1898, Bruce gave a careful and full account of similar observations in which also the Marchi method was available. With much of the description of this author we are in agreement, but some interesting points not shown in his figures will be described in this paper. A contribution on the same subject has recently been published by Risien Russell.[1]

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[1] BRAIN, Summer, 1898.

The first case was one of caries of the spine, in which microscopical examination showed that at the level of the lesion in the mid-thoracic region, the cord was completely disintegrated.

The other case was a severe crush, the cord being entirely destroyed at the level of the tenth dorsal segment, with extensive consequent myelitis. There was also severe damage to the fourth posterior cervical root on the left side.

The tissues after hardening in Müller's fluid were stained by the Marchi method and sections cut after paraffin embedding.

(I.) *Postero-median column.*—The postero-median column, including the septo-marginal tract of Bruce and Muir was completely degenerated as high as the funiculus gracilis. It ended entirely in this nucleus. In the lowest cervical region the degeneration extended markedly up to the posterior commissure and spread along it as far as the margin of the posterior horn, thus embracing the cornu-commissural zone of Marie (fig. 1).

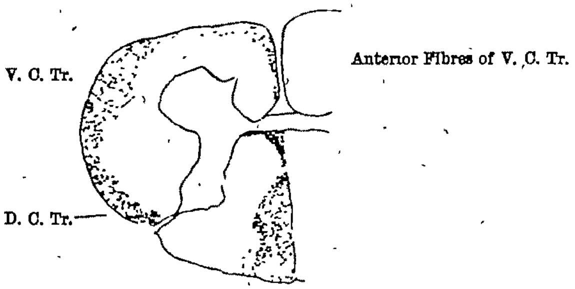

FIG. 1.
Spinal cord at the fifth cervical segment.

At the level of the fourth cervical root this appearance was much less marked (fig. 2), and just below the decussation (fig. 3) the area had assumed a distinct wedge shape, this feature being in accordance with Singer's law.

(II.) *Dorsal cerebellar tract.*—The course of this tract in the spinal cord is well seen in figs. 1, 2, 3. In this situation it has the position usually described. Sections in

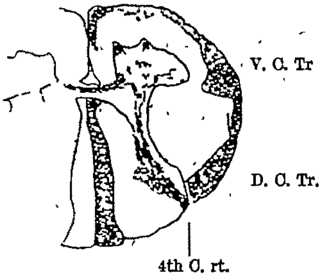

FIG. 2.
Spinal cord at the fourth cervical segment.

the lower cervical regions show that it is closely applied to the posterior horn, spreading inwards along its outer border for a considerable distance. In the lower medullary region (figs. 4 and 5) it forms, together with the ventral cerebellar tract a well defined wedge-shaped area just anterior to the substantia gelatinosa of the fifth nerve.

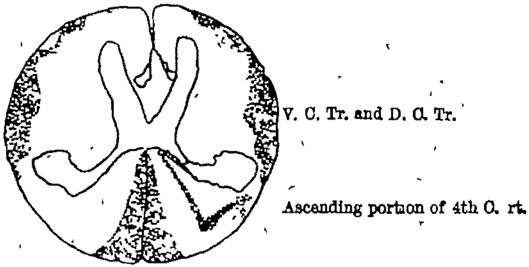

FIG. 3.
Spinal cord at the lower limit of the pyramidal decussation.

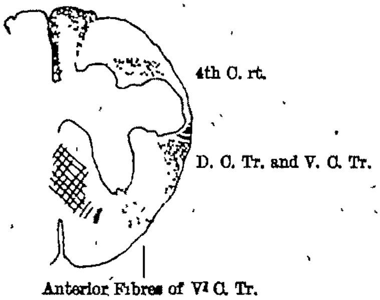

FIG. 4.
Medulla below the olivary body.

In our sections a distinct peripheral band of degenerated fibres is seen to connect this area with the degenerated fibres of the funiculus gracilis. We have not seen such a condition described elsewhere, and are in doubt whether to consider all these degenerated fibres as part of the dorsal cerebellar tract.

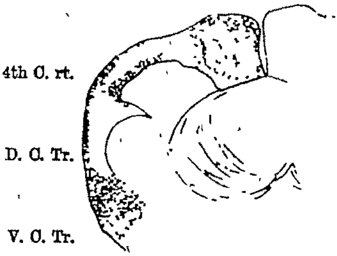

FIG. 5.
Medulla at the lower limit of the inferior olivary body.

In fig. 6 the tract occupies the central part of the corpus restiforme in a position described by other authors, and in fig. 7 it is seen passing into the cerebellum. We regret that we have been unable to trace its further destination.

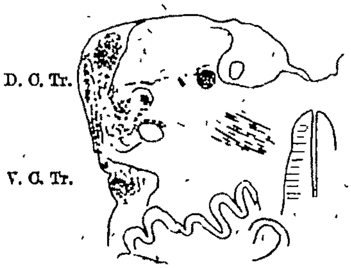

FIG. 6.
Medulla at the middle of the olives.

(III.) *Ventral cerebellar tract.*—The position of this tract in the spinal cord is shown in figs. 1, 2, 3. The main portion of the fibres form a wedge-shaped area opposite to the lateral part of the anterior horn, extending close up to the periphery. This peripheral situation differs from that given by Risien Russell,[2] but is in agreement with the description of other authors. A marked feature in our sections is the presence of a considerable number of degenerated fibres occupying the periphery of the most anterior part of the white matter, and dipping down along the anterior fissure.

Degenerated fibres in a similar position have been noted by Sherrington[3] in the monkey after complete transection of the cord.

This condition in the human cord does not appear to have been noted by other writers. Tracing these fibres upwards it is seen that the formation of the pyramids pushes them backwards. At this level (fig. 4) the greater part of the fibres pass inwards and become dispersed in the white matter between the posterior border of the pyramid and the lateral nucleus of the medulla. Our sections do not give positive evidence whether these fibres terminate in the lateral nucleus or not, but such a condition appears probable.

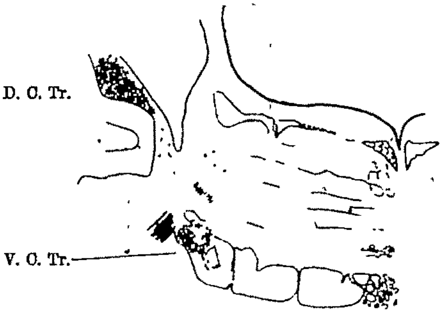

FIG. 7.
Pons at the exit of the fifth nerve.

In fig. 6 the main part of the ventral cerebellar tract is seen just external to the inferior olive. In fig. 7 it is placed more deeply, just ventral to the outgoing fifth nerve. In fig. 8 it is seen curving round the superior peduncle of

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[1] *Journ. of Physiology*, vol. xiv., 4 and 5.
[2] *Loc. cit.*

the cerebellum, and entering the superior medullary velum in an identical position to that described by Bruce. A few degenerated fibres were found at a slightly higher level, but the material at our disposal unfortunately did not allow of our determining whether these passed to the inferior corpora quadrigemina.

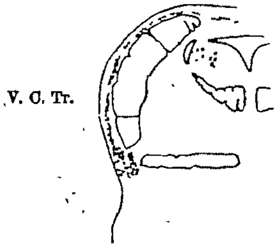

FIG. 8.
Pons at its upper limit.

(IV.) *Spinal portion of the fourth posterior cervical root.*—In one of the preceding cases this root was considerably damaged, and by means of the Marchi method its course could be accurately traced.

(*a*) *Descending portion.*—This is found to occupy an elongated zone in the middle of the postero-external column. It is well marked in the middle of the fifth segment, and scattered fibres can be traced as far as the lower part of the sixth segment. Throughout their descending course these fibres give off collaterals to the posterior horn.

(*b*) *Ascending portion.*—Fig. 2, which is at the level of the injured root, shows the entrance of degenerated fibres into the postero-external column, and the rich distribution of the reflex collaterals of Kölliker, which appear to be chiefly directed towards the postero-lateral group of cells. Other evidence tends to show that this group of cells receives special innervation from the posterior afferent root fibres. The collaterals are confined to the same side as the root lesion, and although more numerous in the fourth segment, are found in the segment above, and also, as previously stated, in the fifth segment.

Fig. 2 further shows a marked degeneration in the anterior commissure. The fibres can be traced from the anterior horn on the side of the lesion to the white matter between the fissure and anterior horn of the opposite side.

This decussating system of degenerated fibres was limited to the region of the injured root. In sections higher up it was not possible to distinguish between these fibres and those previously noted, which are in relation to the ventral cerebellar tract. Under the name of "crossed afferent tract" Edinger describes in this position a system of fibres, whose origin is from the posterior roots, ascending to terminate in the corpora quadrigemina or optic thalamus. Observers (Mott and Langley) who have noted this tract in experimental cases are divided in their opinion as to whether the fibres take origin in the posterior roots or in the most dorsal segment of the posterior cornu.

In our case there was no indication that the posterior cornu was injured, and hence this observation tends to confirm Edinger's view.

Sections (fig. 2) at the site of the injured nerve also showed distinct degeneration in some fibres passing from the anterior horn, which were limited to the side of the lesion. These fibres were too numerous to be neglected, but it did not appear that they were continuous with those entering the posterior horn. We are therefore unable to give a definite opinion as to their precise meaning.

The ascending portion of the fourth root in the third and higher segments occupies (fig. 3) an elongated area in the median part of the postero-external column, extending ventrally as a narrow strip to the base of the posterior horn, while dorsally the area widens and curves outwards towards the posterior root zone. In figs. 4 and 5 the fibres are seen collected around the external cuneate nucleus in which they end.

A STATISTICAL INQUIRY INTO THE PREVALENCE OF EPILEPSY AND ITS RELATION TO OTHER DISEASES.

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THE following paper is based on an inquiry into the occurrence of epilepsy or epileptiform convulsions in the family or personal history of 5,000 patients, who at the time of the inquiry were complaining of other than epileptic disease. From the results so obtained I have endeavoured to ascertain what, for want of a better term, may be called the average accidental incidence of epilepsy in family and personal history, and thus establish a standard from which the part, if any, played by epilepsy in the predisposition to other diseases may be decided.

The term "accidental" must not be accepted too literally. There are certain diseases, such as insanity, chorea, and some chronic nervous diseases, with the liability to which an epileptic inheritance or the occurrence of past personal epileptic fits has an established relation. In these cases, therefore, the patients will give a personal or family history of epilepsy in numbers altogether in excess of those met with in the case of such disorders, for example, as the specific fevers or diseases of the skin, with which epilepsy has apparently no relation at all. Nevertheless, a certain small proportion of the latter patients will give an epileptic history, owing to the fact that epileptics and those inheriting a family tendency to epilepsy are at least as liable to contract such disorders as other more healthy individuals, and it is to express this fact that I have used the term accidental. Yet I do not intend to assert that the relationship between epilepsy and these disorders is necessarily of an entirely accidental character, for it is always possible that the epileptic taint may be one of a long series of links in the chain of causation. Indeed, my figures give some support to this idea.

Besides perhaps throwing some additional light on the natural history of epilepsy, there are certain disputed points which can only be decided by such an inquiry. For example, it is still a moot point whether phthisis and epilepsy have any special relationship with one another. Sir William Gowers obtained a phthisical family history in 39 per cent. of 200 epileptic patients, but came to the conclusion that the frequency of this association might probably be accounted for by the wide-spread diffusion of phthisis; whilst Dr. F. Roberts, who at his request investigated the matter from the other point of view, found that an epileptic family history was only forthcoming in 2·5 per cent. of his phthisical cases, a percentage which he thinks is not above the average. But these figures are inconclusive owing to the lack of any standard with which they can be compared, and which gives the incidence of phthisis and epilepsy in other cases of disease. A knowledge of the average occurrence of epilepsy, which it is the object of this paper to establish, will, of course, determine only one side of these and similar questions; but I have endeavoured to obtain some statistics as to the prevalence of phthisis also, and thus to decide the relationship of that disease to epilepsy from both points of view.

Method of the Inquiry.

The 5,000 cases on which the epileptic statistics are based were obtained entirely from my own out-patients. They therefore all belong to the same class of society, and are practically consecutive. Each patient on his first attendance was asked as to the existence of "fits" in his family or personal history, and the case with its result entered under the corresponding diagnosis. It is of course true that in the hurry of a crowded out-patient department diagnosis is often of a somewhat rough description. Nevertheless, I have taken the greatest possible care to obtain accuracy, and have freely revised the diagnoses as occasion has demanded. Moreover, whenever the diagnosis has seemed to be doubtful, I have excluded the case from any of the definite groups and have placed it in a separate list reserved for cases of a doubtful nature. I therefore venture to believe that no very serious error has crept into the results from this source.

The inquiry for the occurrence of "fits" has necessarily elicited a history of hysterical as well as epileptic convulsions. My table therefore includes both varieties. It is often, however, a most difficult matter to distinguish between epileptic and hysterical fits from the account of an uneducated person, and in no less than 20 per cent. of all the fits of which a history has been given, I have been entirely unable to decide to which category they should belong. In these cases, therefore, the fits have been placed in a separate group under the heading "Doubtful." In the remaining 80 per cent., in which I have arrived at a conclusion one way or the other, I believe that I have had good grounds for my decision.

The points on which I have relied in attempting to distinguish between the two sets of convulsions are those usually accepted. Thus, I have taken as fairly conclusive of epilepsy, tongue-biting, passage of urine or motions in the fits, and occurrence of serious bodily mischief, such as bad burns or scalds, and really bad falls, &c., though I am, of course, aware that such accidents are not absolutely conclusive against hysteria. Detention in a lunatic asylum has also as a rule been taken as evidence that the fits were of an epileptic character. Again, in not a few cases my informant has given me so good an imitation of the movements of an epileptic fit as to convince me of its nature. On the other hand, screaming, fighting and struggling, talking, crying, and banging the head, have been accepted, with other points, as evidence of hystero-epilepsy. Leading questions have in all cases been as far as possible avoided.

In some cases there has seemed to be a fairly clear history of the occurrence at different times of both varieties of fits. This is only in accordance with the well-known tendency of the two conditions to occur in association with one another.

Whatever pains be taken, however, in the examination of the point, some mistakes in interpretation will probably occur. In order to minimise the difficulty as far as possible, I have given in the two final columns of the table, first, the total number of personal fits of all sorts (epileptic, hysterical and doubtful added together), and secondly, the sum total of all the fit histories, family as well as personal, hysterical and doubtful as well as epileptic. In these columns, at any rate, there is no room for fallacy.

No notice has been taken of any fits occurring in the descendants of the patients, owing to the possibility of the inheritance arising from the other parent. Moreover, no fits occurring in individuals under three years of age have been registered, nor any for which the action of a poison or source of irritation might have been responsible. The personal fits of patients suffering from Bright's disease, lead poisoning, worms, &c., have therefore been omitted, unless they occurred at a period previous to the exposure to the poison or irritation.

Finally, it must be remembered that the figures undoubtedly understate the incidence of both varieties of fits, owing to the very imperfect knowledge of family history prevalent amongst the working classes. Both epileptic and hysterical inheritance must therefore be more frequent than is shown by my figures.

Arrangement of Statistics.

The cases are arranged under twenty-one different diagnoses, one additional group being added under the heading "Various." The latter contains all the disorders the representatives of which have not amounted to seventy-five in all, this being taken as the smallest number which would justify separate analysis. Another group originally contained cases of doubtful diagnosis, but this has now been added to the "Various" cases.

Some of the groups need a brief explanation :—

Anæmia.—This group is made up entirely of young women, mostly from 15 to 25 years of age. All special forms of anæmia, with the exception of chlorosis, have been placed in the "Various" group.

Bright's disease.—The different varieties of Bright's disease have all been classed together, seeing that their separate analysis has given closely similar results.

Dyspepsia.—The dyspeptic group contains undoubtedly a very miscellaneous set of cases. I have, however, endeavoured to simplify it by separating the male from the female cases, holding that the latter constitute a far more neurotic group. It is still the case that very various forms of stomach upset are included under the same heading, but it would be somewhat hazardous to attempt much subdivision.

Debility.—The patients here consist largely of the over-worked and underfed men and women who are met with constantly in hospital practice in large manufacturing towns. They were suffering from no ailment which would place them in any of the other groups.

Headache.—No patient has been included in this class in whose case a definite cause could be assigned for the complaint. The cases are those of so-called functional headache.

Nil.—In this group have been placed those patients with whom a careful examination has convinced me that there has been little or nothing the matter.

Rheumatoid arthritis.—Under this head a few cases of chronic "rheumatism" other than rheumatoid arthritis have probably been included.

Various.—As already explained, this class contains the diseases the representatives of which have not amounted to seventy-five in number, and also cases of doubtful diagnosis:

Results Arrived at.

The table of results is as follows :—

	Cases.	Ep. Fam. Hist. Per cent.	Ep. Personal. Per cent.	Ep. Fam. and Personal. Per cent.	Hyst. Personal. Per cent.	Hyst. Fam. and Personal. Per cent.	Doubtful. Per cent.	Total Personal. Per cent.	Total Fits. Per cent.
Anæmia	431	4·4	0·9	5·1	2·8	8	2·6	5·1	14·6
Bright's Disease	136	2·2	1·5	3	0·7	3	2·2	3	8·8
Acute Bronchitis	137	4·4	4·4	7·3	0·7	4·3	2·2	5·8	13·9
Chronic „	211	3·8	2·8	4·7	0	0·5	2·4	3·3	7·5
Chorea	146	17·8	6·2	21·2	1·4	6·2	2·1	7·5	25·3
Dyspepsia (Male)	130	1·5	0	1·5	0	4·6	2·3	0·8	8·4
„ (Female) ..	375	5·1	1·6	6·7	2·4	6·9	1·6	4	13·3
Debility	183	5·6	1·1	5·6	0·6	3·9	2·8	2·2	11·7
Fevers	114	3·5	0	3·5	0·9	3·5	0·9	1·8	7·9
Headache	131	10·7	3·1	13	1·5	3·8	4·6	7·6	20·6
Heart (Valvular)	169	4·7	4·1	8·3	0	4·1	0·6	5·3	13
„ (Muscular)	77	5·2	1·3	6·5	1·3	2·6	0	2·6	7·8
Myalgia	123	7·3	0	7·3	0·8	4·9	2·4	3·3	13·8
Neuritis	75	6·7	0	6·7	0	2·7	2·7	1·3	10·7
Neuroses	321	5·9	1·9	7·5	2·8	7·2	1·9	5	15·3
Chronic Nervous Diseases	111	9	4·5	11·7	0·9	2·7	1·8	5·4	14·4
Nil	136	2·9	0	2·9	0	0·7	0·7	0	4·4
Phthisis and Chr. Pneum.	276	6·2	4·3	10·1	0·7	3·3	0·7	4·7	13·8
Acute and Subacute Rheumatism	132	4·6	2·3	6·1	2·3	4·6	2·3	5·3	12·1
Rheumatoid Arthritis ..	87	8	1·1	8	0	0	2·3	3·4	10·3
Skin Diseases	174	3·4	0·6	4	1·1	4·6	2·3	2·8	10·3
Tonsillitis, Pharyngitis and Stomatitis	127	4·7	1·6	4·7	1·6	3·9	0·8	3·1	7·9
Various	1198	4·2	1·1	5·2	0·8	3·2	1·8	2·3	10
Total (Average)	5000	5·2	1·8	6·6	1·1	4·2	1·9	3·6	11·9

Note.—In order to save multiplication of columns, Family History includes patient's own generation as well as preceding generations.

The chief point of interest of the average thus obtained lies in the frequency with which it shows that fits of one sort or another occur amongst the working classes. Thus, no less than 11·9 per cent. of my out-patients, excluding those attending directly for epilepsy or hystero-epilepsy, gave me a family or personal history of fits, whilst 3·6 per cent. had suffered from fits themselves at some period of their lives; 5·2 per cent. gave a family history of epilepsy, and 1·8 per cent. had themselves had epileptiform convulsions. It has already been noted that the figures understate the case as far as family history is concerned.

The average is inaccurate, however, if it be taken to represent the extent to which personal and family histories of epilepsy and hystero-epilepsy are to be found amongst persons who are suffering from complaints with which these disorders have no recognised relation; for the cases on which the epileptic average is based include both chorea and the chronic nervous diseases, and the hystero-epileptic average is similarly invalidated by the inclusion of anæmia, the neuroses, and the female cases of dyspepsia, with all of which hysteria may be accepted as possessing a definite relation. Headache, again, has an easily understood relation to both epilepsy and hystero-epilepsy; whilst finally it is known that epileptiform convulsions are not uncommon complications of valvular heart disease. Hence, the first step towards obtaining the true "accidental" incidence of epilepsy and hystero-epilepsy must be to subtract all the above-mentioned conditions, and to take the average of those remaining. The average now stands as follows, the items being arranged in the same order as that adopted in the table:—

3306 4·4 1·5 5·6 0·7 3·2 1·8 2·8 10

I do not, however, think that even this represents accurately the average at which I wish to arrive. On studying the table certain diseases are seen to stand out, as regards the incidence of epilepsy distinctly above the corresponding figures in the last obtained average. These diseases are phthisis and chronic pneumonia, and acute bronchitis, as regards epileptic personal history, and acute and subacute rheumatism as regards the total number of personal fits of all sorts. To these I should also add rheumatoid arthritis as regards epileptic family inheritance, were it not that there is a complete absence here of any record of hysterical fits, and that the total fit incidence is scarcely above the average. These facts suggest that a larger number of cases would probably level the average by the inclusion of cases of hystero-epilepsy. The group of myalgias also claims removal on the ground that it exceeds the average as regards both family epileptic inheritance and the total fit incidence; but, although the connection of these cases with rheumatism might possibly justify me in dealing with them in the same way as the above mentioned diseases, the group is perhaps somewhat ill-defined, and is, therefore, better retained.

At the risk of appearing to assume the points under discussion, I yet think that the cases of phthisis, chronic pneumonia, acute bronchitis, and acute and subacute rheumatism must be withdrawn in order to arrive at the final accidental incidence of epilepsy; for, if my figures be correct, they afford some evidence that these conditions stand to it in some special relation. In other words, they are now under suspicion. If they have no such special relation, their removal should not affect the results; and if, on the other hand, they do stand in some special relation, their retention in the table clearly vitiates the average. The final "accidental average" therefore now stands as follows :—

Cases.	Ep. Fam. Hist Per cent.	Ep. Personal. Per cent.	Ep. Fam. and Personal. Per cent.	Hyst. Personal. Per cent.	Hyst. Fam. and Personal. Per cent.	Doubtful. Per cent.	Total Personal. Per cent.	Total Fits. Per cent.
2768	4·3	1	4·9	0·7	3·1	1·9	2·3	9·5

These figures give, I think, the "accidental" incidence of epileptic and hysterical convulsions as nearly as it can be arrived at.

Provisional Inferences.

On comparing this average with the figures in the table, the following points are to be noted :—

Anæmia.—The epileptic incidence is almost identical with the average, but the persónal and total incidence of hysterical convulsions show a considerable increase—namely, 2·8 and 8 against 0·7 and 3·1 per cent. respectively.

Acute bronchitis.—The personal epileptic fits stand at 4·4 instead of 1 per cent. The percentage of personal fits, all sorts included, is 5·8 as compared with the average of 2·3.

Chronic bronchitis.—In contra-distinction to the total fit incidence of the cases of acute bronchitis (13·9 per cent.), the total liability is here below the average (7·5 instead of 9·5 per cent.). It is however to be remarked that even here the average of personal epileptic fits is nearly three times the normal (2·8 as compared with 1), whilst the total personal fits stands at 3·3 instead of 2·3 per cent.

Chorea gives the largest epileptic incidence, and shows some increase also in hysterical relationship. The total incidence is 25·3 instead of the average 9·6 per cent.

Headache gives the next largest percentage of fit incidence of all classes. The family epileptic percentage is 10·7 compared with the normal 4·3; the personal epileptic incidence is 3·1 instead of 1 per cent. Taking fits of all sorts together, the personal percentage is 7·6 compared with 2.3, and the total 20·6 instead of 9·5.

Heart (valvular.)—The figures here obtained support the view that patients suffering from cardiac valvular disease are more subject to the occurrence of eleptiform fits than other people. Thus, personal epileptic fits were noted in 4·7 per cent. of the patients, as compared with the average of 1 per cent.; and in 2·4 per cent. there was good reason for thinking that the fits had occurred after the onset of the endocarditis. In 1·2 per cent., however, this was certainly not the case; whilst in the remaining 1·2 per cent. there is no evidence on the point one way or the other.

Neuritis.—The only point to be noticed in this group is a moderate increase in the epileptic family inheritance.

Neuroses show an increase in the total personal fits (5 per cent. instead of 2·3), whilst the percentage of fits of all sorts combined is 15·3 instead of 9·5. The increase is here chiefly on the hysterical side, though there is also some excess of epileptic inheritance.

Phthisis and chronic pneumonia give a moderate increase in epileptic family history (chiefly, however, in the patient's own generation), and a marked increase in the number of personal epileptic fits (4·3 instead of 1 per cent.). Taking the personal fits of all sorts and the total combined fits, the numbers are 4·7 and 13·8 as compared with the normal of 2·3 and 9·6 respectively.

Acute and subacute rheumatism.—There is again a marked increase in the total number of personal fits, those due to epilepsy and hysteria being now equal in number. But I have unfortunately omitted to note the condition of the heart in many of these cases, and the part played by this factor is therefore uncertain. The relation of rheumatism thus needs further investigation.

Chronic nervous diseases.—It is unfortunately useless to split this group up into the separate diseases of which it is composed, for the number of cases in each category is too small for individual analysis. There is, as would be expected, a great increase in both family and personal epileptic incidence.

Speaking provisionally—for some of the suggestions need the support of a larger series of cases—the foregoing points give some ground for thinking that the various disorders may be arranged in an ascending scale according to the degree to which the family and personal histories of the patients are tainted with epilepsy.

(1) It is to be noted that the group ("Nil") which includes the individuals nearest to a normal state of health, gives a far lower fit incidence than that of any of the other groups. This incidence amounts to but 4·4 per cent. for fits of all classes, no personal fits of any sort being registered. There appears, therefore, to be some reason for believing that an inquiry into the history of a perfectly healthy set of persons would give a uniform average of fit incidence much lower than that to which the name accidental has hitherto been applied. The "accidental average" must therefore be considered as applying to the sick members of the working population only.

(2) More than 50 per cent. of the more definitely ailing patients give a fairly uniform average of epileptic incidence —that, namely, established in my final average.

(3) A group including acute (? also chronic) bronchitis, phthisis, chronic pneumonia, valvular heart disease, and acute and subacute rheumatism, shows a striking increase in the number of patients who have themselves suffered from epileptiform convulsions.

(4) Finally, the most marked epileptic incidence is to be found in the cases of chorea, functional headache, and chronic nervous disease, in all of which the relationship reaches a high degree.

Cases of Lung Disease.

One of the chief points of interest in the above conclusions lies in the apparently large number of patients affected with phthisis, chronic pneumonia, and acute bronchitis, who have suffered from epileptiform convulsions. I therefore give a few further details concerning these cases.

A possible source of fallacy as regards the phthisical cases lies in the fact that they are practically exposed to an age limit, whereas the cases with which they are compared include patients of all ages. Thus, in the phthisical cases there are but very few patients below the age of 15, and it is clear that in order to bring the accidental average into strict comparison with the phthisical average, all patients under this age should also be omitted. This correction, however, only brings the accidental average of personal epileptic fits up to 1·1 instead of 1 per cent., whilst the percentage of total personal fits of all sorts is changed from 2·3 to 2·5 only. The removal of this fallacy therefore, does not materially affect the result. In the cases of bronchitis no such correction is needed.

Again, I have looked carefully into the history of the individual fits in the phthisical and bronchitic patients, in order to see how they compare from the point of view of permanancy with the personal fits of which a history has been obtained in the whole series of 5,000 cases. The result is as follows:—

Personal epileptic fits occurring amongst the 4,597 patients who were not suffering from either phthisis or bronchitis:—

Confirmed Epilepsy, Past or Present.	Recent only.	Former and Temporary.
67·1 per cent.	19·7 per cent.	13·1 per cent.

Personal epileptic fits occurring amongst the 137 cases of acute bronchitis :—

Confirmed Epilepsy, Past or Present.	Recent only.	Former and Temporary.
83·2 per cent.	16·6 per cent.	0

Personal epileptic fits occurring amongst the 265 cases of phthisis, &c. :—

Confirmed Epilepsy, Past or Present.	Recent only.	Former and Temporary.
69·3 per cent.	15·4 per cent.	15·4 per cent.

It is therefore clear that the proportion of cases of confirmed epilepsy is materially above the average in the bronchitic cases, and slightly above it in the cases of phthisis.

The cases are as yet too few for any certain conclusions to be drawn, but the inference is strongly suggested that those patients whose nervous constitution is a weak one—as shown by the inheritance of an epileptic tendency, and especially by the occurrence of epileptic fits in the patients themselves—are directly predisposed to the development of serious lung mischief. The point needs, however, to be supported by a larger number of cases.

Inheritance of Phthisis by Epileptic Patients.

The establishment of the average inheritance of phthisis by hospital patients is an extremely difficult matter, owing to the looseness with which the term consumption is used to and by the working classes. The following table, based upon an inquiry into this point in the case of 2,966 patients, must therefore be taken with considerable reserve, as representing but little more than the mere statements of the patients as to the existence in their families of a history of phthisis. In all cases supporting evidence, such as hæmoptysis, has been asked for, but in a large minority it has been necessary to take the statements without corroboration. The arrangement of the table is the same as before :—

	Cases.	Phthisis Inherited. Per cent.		Cases.	Phthisis Inherited. Per cent.
Anæmia	249	23·3	Heart (Muscular) ..	46	17·4
Bright's Disease ..	96	9·4	Hystero-Epilepsy ..	17	46·5
Acute Bronchitis	67	25·4	Myalgia	68	14·7
Chronic Bronchitis	118	13·6	Neuritis	48	14·6
Chorea	78	26·9	Neuroses	165	15·1
Dyspepsia (Male)	85	4·7	*Nil*	94	21·3
Dyspepsia (Female)	218	16·1	Chronic Nervous Dis...	57	14
Debility	97	18·6	Phthisis	149	31·6
Epilepsy	114	27·1	Acute & Subac. Rheum.	75	16
Fevers	57	26·3	Rheumatoid Arthritis..	50	20
Headache	66	10	Skin Diseases	118	17·8
Heart (Valvular)..	96	17·4	Tonsilitis, &c.	75	13·3
			Various	680	17

Total .. .. .. 2,966 .. 18·1 per cent.
Total (excluding Phthisis) 2,817 .. 17·4 per cent.

According to this table, it would appear that epileptic patients give a large inheritance of phthisis (27·1 per cent.). But the great irregularity of the results deprive this fact of much of its value. Thus, the specific fevers give a scarcely smaller inheritance—namely, 26·3 per cent., though the small number of cases may perhaps to some extent explain the difficulty. As far as it goes, however, the table supports the view that an inheritance of phthisis predisposes to the occurrence of epilepsy. It may be added that a similar belief—namely, the connection between chorea and tuberculosis—receives support from this table.

The general conclusion thus seems to be in favour of the view that epilepsy and phthisis have some connection with one another from both points of view. This conclusion, as far as epileptic incidence in the histories of phthisical patients is concerned, is not in accordance with that arrived at by Dr. F. Roberts, and quoted at the beginning of my paper; for although this observer did not inquire into the occurrence of epileptiform convulsions in the personal histories of his patients, he found an epileptic family inheritance in only 2·5 per cent., as compared with the percentage of 6·2 obtained amongst my own phthisical patients. I cannot explain the discrepancy, but it appears to me possible that the explanation may to some extent lie in the different conditions of life obtaining in London and in a large manufacturing town such as Birmingham, and perhaps in some difference in the class of society from which the patients are drawn in the two cases.

A CASE OF ACUTE MENINGO-MYELITIS.

BY E. F. TREVELYAN, M.D.

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SUMMARY:—Man, aged 37, exposed to severe cold on March 22. Great pain in the back from March 24 to April 11. Retention of urine on April 11, and rapid loss of power in the legs two days later. Complete flaccid paraplegia with sensory paralysis and loss of knee-jerks. Unexpected death from cardiac failure on the eighteenth day of the disease. Suppurative external meningitis in the dorsal region. Intense and mostly patchy myelitis from D 3 to L 3. Pus in the muscles of the back. A small localised empyema. No vertebral disease.

The following are short notes of the case.

A previously strong and healthy man, aged 37, was paving in Leeds on March 22, 1898—a snowy and bitterly cold day. On March 24 there was severe pain in the back, intermitting and stabbing. The pain was worse when he straightened himself after stooping. He gave up his work on April 9 for Easter. During the holiday he walked about, but often had the pain in his back. There was no pain or tingling in the legs. On April 11 he was unable to pass his urine. A little urine dribbled away on the 12th. The distension of the bladder caused him much pain. The bowels were very constipated. On April 13 the patient was catheterised and the catheter was used on five occasions before his admission into the Leeds General Infirmary on the 15th. On the evening of the 13th he got out of bed and quite suddenly lost the use of his legs and fell to the ground. Sensation was said to have been lost at the same time. During the night fæces were passed unconsciously into the bed. I saw the patient on the 14th with Dr. Spong, of Leeds, and he was admitted into the Infirmary on the following day. There was a history of syphilis fifteen years previously—a chancre, but no secondary symptoms; treatment was continued for thirteen weeks.

On admission.—The lower extremities were helpless and he could only alter the position of the trunk with difficulty, chiefly owing to the pain in the back. There was retention of urine and the stools were passed unconsciously. Pain was complained of round the chest about six inches above the umbilicus. The pain was not continuous, but of a tearing character and most intense in the epigastric angle. Above this level there was a zone of hyperæsthesia, and below it loss of sensation. The *legs* were completely paralysed so that not even the toes could be moved. The muscles were fairly well nourished but flabby. They were not tender. The superficial and deep reflexes were absent. Sensation was almost completely lost; the patient could not feel the prick of a pin or tickling the soles, but he could just feel a sharp rub against the leg. Sensation to heat and cold was quite abolished. There were no trophic disturbances. The *arms* were unaffected. There was no undue prominence of the spine. There was much tenderness over the lower dorsal vertebræ, and pain was complained of when a deep breath was taken. The patient also complained of inability to cough up the expectoration which now and again accumulated. The examination of the chest as far as it was possible to make it gave negative results. The urine, specific gravity 1029, acid, contained mucus but no albumen. April 21.—The patient's condition is unchanged. The urine remains strongly acid. April 26.—Condition much as before. He sometimes feels a tingling in the legs, especially the right. The anæsthesia begins just below the distribution of the sixth intercostal nerve. The temperature rises in the evening. The patient was in much the same state until the early morning of the 28th, when he was seized with cardiac failure and died on the eighteenth day of the acute myelitis and the thirty-sixth day of the disease.

POST MORTEM.

The brain weighed 42½ ozs., and no evidence of disease was found in it. The meninges were healthy.

Spinal cord.—In the middle and lower parts of the dorsal region there was dirty looking pus on the outer aspect of the dura mater. The pia mater appeared healthy. Parts of the cord were obviously softened. Only one incision was made into it, and that through the lower dorsal region, where there was some bulging. The cord was almost diffluent here. The muscles of the back were infiltrated with pus, especially on the left side. A very small empyemal cavity containing offensive pus was found close to the vertebral column on the right side. The lungs were otherwise healthy. The bladder was large and its walls thin, but the mucous membrane healthy. There was no evidence of cystitis. The kidneys were large, somewhat engorged with blood, but otherwise healthy. There was no pus in the ureter or pelvis of the kidney. The heart, including the valves, was healthy. The spleen was a little enlarged. The liver was also slightly enlarged, and adhesions were found between it and the diaphragm. These organs were otherwise healthy. Cultures were prepared from the pus outside the dura mater, and also from a softened patch in the cord. The same micro-organism (a large diplococcus) was obtained from both these lesions. The bacteriological examination was unfortunately not carried further, as the micro-organism died in a few days.

The whole cord was hardened in formol-Muller, and was divided into its segments. Portions from each segment from D 3 to L 4 inclusive were embedded in paraffin, the other parts of the cord being sufficiently firm to cut without embedding. Later each segment was again divided into pieces measuring about 2 mm., and the situations of the lesions as then seen were carefully noted.

The naked eye appearances of the cut sections of the hardened cord will first be described, as the lesions stood out very prominently. The results thus obtained were carefully compared with the changes observed in microscopical preparations from all parts of the cord. It is, of course, not assumed that the lesions visible to the naked eye corresponded exactly to the morbid change as seen under the microscope; but there was a very general agreement between the two. The disease was certainly of the disseminated and patchy type in nearly all parts of the diseased cord, and healthy nervous tissue was found between the patches. Sometimes these patches were very sharply defined from the healthy tissue as in D 4, but at other times the one faded more gradually into the other.

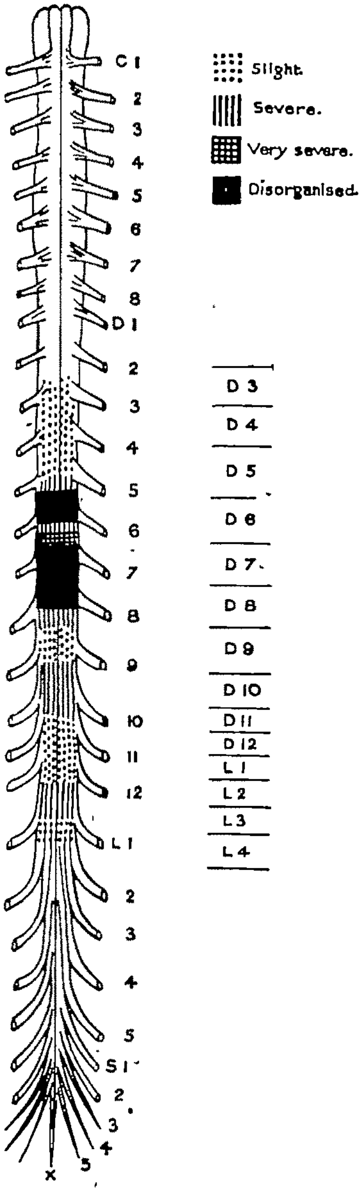
In its *longitudinal* distribution the disease was traced from D 3 as low down as L 3. The most intense disease was found in the lower part of D 5 and upper part of D 6, and again throughout D 7 and in the upper part of D 8. Here no distinct structure could be recognised by the naked eye, and an advanced disorganisation of the cord was made out by the microscope. Above D 3 there was an ascending degeneration, but no descending lesion could be ascertained in that part of the cord below L 3.

In its *transverse* distribution the disease was distinctly patchy, except where marked disorganisation was present. These patches were more numerous in the upper part of D 6, where in some places as many as nine patches could be counted in the cross section of the cord. In D 4 and 3 the disease was represented by a single, well-defined focus at the junction of the right anterior and posterior horns. Towards the lower limit of the lesion in the lumbar cord the patches were almost exclusively confined to the posterior columns or immediately adjacent parts. These patches were, generally speaking, much more abundant in the periphery of the cord than in the central parts, that is, they were placed in the peripheral circulation. At the upper limit of the lesion the patches were more centrally placed.

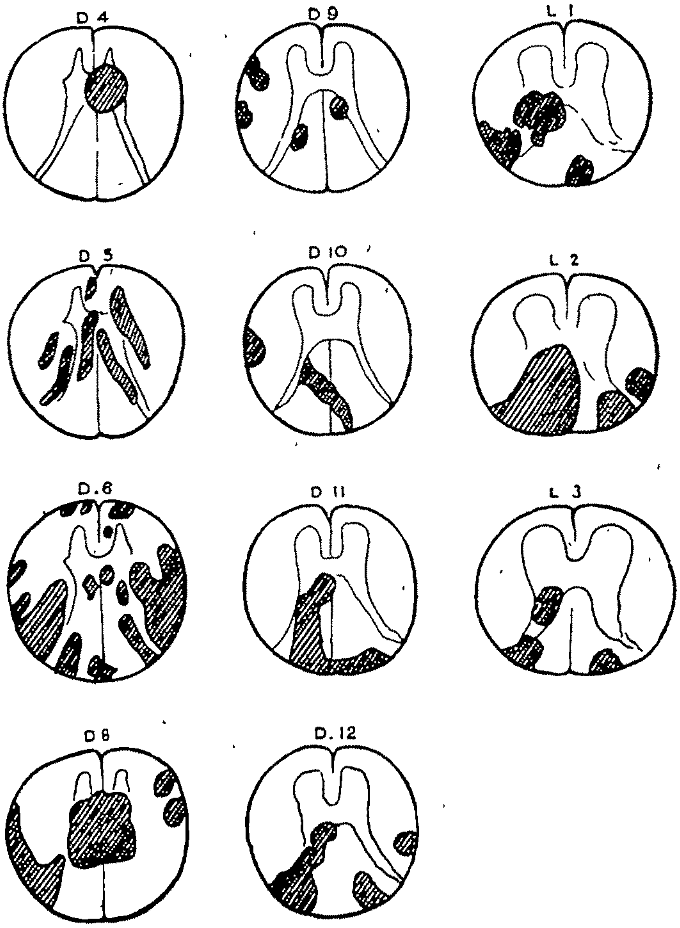
No distinct naked eye lesion could be made out in the hardened medulla oblongata, pons, cerebellum or cerebrum.

As regards the microscopical appearances, it must, of course, be borne in mind that the case terminated on the eighteenth day. The most marked changes were certainly centred in the parenchymatous elements.

There has been a great destruction of ganglion cells throughout the diseased portions of the cord; in fact, very few healthy ones are to be seen. Even in the lower lumbar segments they are considerably involved. Here the cells have lost their processes—have become rounded and translucent-looking, and the nucleus and nucleolus have disappeared. Neither vacuolation or pigmentation is seen. The nerve-fibres, including the axis-cylinders, are greatly altered in the diseased parts. Sometimes the axis-cylinder is so swollen that only a thin layer of


C 1
2
3
4
5
6
7
8
D 1
2
3
4
5
6
7
8
9
10
11
12
L 1
2
3
4
5
S 1
2
3
4
5
x
Slight.
Severe.
Very severe.
Disorganised.
D 3
D 4
D 5
D 6
D 7
D 8
D 9
D 10
D 11
D 12
L 1
L 2
L 3
L 4

altered myelin surrounds it. At other times the breaking up of the myelin sheath is very obvious. In some places the nerve-fibres have largely perished, leaving hardly anything more than the glia network. The alteration in the interstitial tissue, including the blood-vessels, is of much interest, considering the undoubtedly infective origin of the disease. Vascular engorgement was not very marked in this



Ascending degeneration in the dorsal and cervical regions. A single small focus of disease in D. 3. D. 7 disorganised. L. 4 healthy.

case. The vessels were, however, here and there crowded with blood-cells, and appeared then to be more numerous than usual (D 6). Very few hæmorrhages were visible; a large one was found in D 10 in the grey matter. No very distinct changes were to be made out in the vessel wall, and none in the perivascular sheath. Hardly any perivascular or other more general infiltration was seen. Thus the changes in the vessels and perivascular tissues are slight.

The changes in the connective tissue, including the neuroglia, were also not marked.

The bands of connective tissue passing into the cord from the periphery are more distinct than usual, and distended blood-vessels may at times be seen in them. There was very little overgrowth of the neuroglia, and in only a few places were spider-cells present in any abundance. Granules were only seen here and there. Large cells with small nuclei, staining by Weigert and other similar methods, were seldom found. Only a few corpora amylacea were present.

It would certainly appear that the stress of the disease, in this case, had fallen on the parenchymatous elements of the cord. If the pathological changes found were due to an infection or intoxication, then the vessels by which the disease-producing agent arrived should show changes in or about their walls; but such changes were only slight in this case. Nor was the lesion limited to any vascular territory, such as would suggest the deleterious action of some poison brought to it by the blood. Although, as mentioned above, the patches were often more abundant in the region of the peripheral blood supply to the cord, they were by no means limited to it.

The bacteriological examination made in this case was far too incomplete to allow of any conclusions being based upon it. Neither the pus of the empyema nor that in the muscles of the back was examined bacteriologically, but the resemblance in the naked-eye appearances of the pus in these two situations was considerable.

It is somewhat difficult to explain the exact relationship between the various lesions found after death, viz., the acute myelitis, external meningitis (without vertebral disease), the small empyema, and the diffuse suppuration in the muscles of the back; but the infective character of these lesions cannot be gainsaid. It is thus difficult to say whether the suppuration outside the vertebral column was primary and the suppurative meningitis secondary, or whether, on the other hand, the suppurative meningitis was primary and the adjacent suppurations secondary. In the allusion to this subject in his well-known text-book, Dr. Gowers recognises the greater probability of the second relationship.

The case illustrates how the disseminated and transverse form of acute myelitis pass into one another. In some parts of the cord there was a total transverse lesion, whereas in other parts the patchy character of the disease was obvious enough.

Finally the symptoms noted during life corresponded very fairly well to the lesions found after death. The intense pain in the back must be largely, if not entirely, attributed to the external meningitis. That all functions dependent on the lumbar and lower dorsal cord were in abeyance is not to be wondered at, considering the intensity and amount of the disease present. The lesion in the cord extended rather higher than the symptoms indicated, but this was no doubt due to the fading off of the disease in a gradual manner from below upwards. Perhaps the unexpected and rapid death was due to minute lesions present in the medulla oblongata and pons. Thus in the region of the nucleus of the tenth nerve very small hæmorrhages were present, but this part of the examination was not as complete as it might have been. Under the circumstances it was almost impossible to recognise the small empyema and the suppuration in the back muscles during life, no doubt chiefly because they were not expected.

FRIEDREICH'S ATAXIA WITH KNEE-JERK SAND ANKLE CLONUS.

BY HOWARD GLADSTONE, M.D., C.M.EDIN.

Late House Physician to the Bradford Royal Infirmary

In February, 1898, Arthur R., a lad of 17, was admitted to the Bradford Royal Infirmary from the out-patient room, suffering from spinal curvature and difficulty in walking. After examination he was found to present all the characters of a case of Friedreich's ataxia. The family history being investigated it was found that his eldest brother, William, was suffering from deformity of the spine, and was unable to stand. He was written to, and a few days later came into hospital with his brother, where they were both under observation for two months, under the care of Dr James Kerr, who has kindly allowed me to record their cases

It is the elder brother's condition which is referred to in the title, for it was found that, while presenting most of the classical features of the disease in a pronounced way, there was ankle clonus on the left side and retention of knee-jerks.

Ankle clonus has not been noted as a sign in any case of Friedreich's ataxia so far recorded, and naturally excites suspicion as to the correctness of the diagnosis. But his brother's case will be recognised as typical, and his own in other respects as strikingly characteristic of Friedreich's disease.

(1) William R., stocking-knitter, aged 24 years, the elder patient, was admitted February 23, 1899.

History.—Symptoms began at 16 years of age, with alteration in the shape of his feet, the instep became high and he could not lace up his boots. At this time he was beginning to grow rapidly. A year later he was taken to the Infirmary, on account of spinal curvature, for which plaster-of-Paris jackets were applied; the deformity nevertheless continued to progress until he ceased growing. His work was trying, for he was obliged to stand all day long in the mill. From 17 years of age he experienced occasionally short stabbing pains in the shin bones. It was not until 18 years of age that he noticed anything wrong with his legs, but then walking became difficult. The difficulty slowly increased, so that fifteen months ago he had to stay at home; he gradually lost the power of standing, and for six months has been unable to do more than crawl about. In addition to the pains in the legs, he had, a year ago, partial loss of sensibility in both thighs; but after two months this was fully restored. No bladder or rectal troubles have occurred. His speech has not been so distinct for the last two years, according to his brother.

Family History.—He is the eldest in a family of six. James, John and Margaret, aged respectively 21, 20 and 19 years, are all healthy. Arthur, 17 years old, is the one who has the same disease, and his case is described later. Mary, the youngest, is 15 years old, and may be another case, for her brother writes that at times she is not steady on her legs. She did not, however, come under our observation. The father, a sergeant, had served nine years in India, but had no disease; he died from acute pneumonia at the age of 54. The mother, 54, is healthy. Grandparents shewed no nervous disease; on the father's side, grandfather is alive, aged 86; grandmother died at 47 of a "weakened heart." On the mother's side, grandfather died at 54, of "chills and dropsy"; grandmother died at 72. In no branch of the family is there any history of nervous disease.

Examination.—Patient has a peculiar physiognomy (figs. 1 and 2). The face is long and narrow, the figure deformed.

Deformities.—There is advanced spinal curvature, of the kypho-scoliotic variety, with the convexity to the right in the dorsal region (fig. 3). The feet show the peculiar deformity characteristic of Friedreich's ataxia (fig. 4). The plantar arch is greatly exaggerated, so that the condition resembles talipes equinus; but there is no contraction of the tendo Achilles or drawing up of the heel; it is a drooping of the front part of the foot, that is, an excessive flexion at the tarso-metatarsal joint. The arching is partly reduced by the weight of the body in standing, but mostly permanent, and due to contraction of the plantar ligaments; he wears ordinary boots, left unlaced over the instep, and his toes enter but a little way into the toe of the boot. The great toes are strung back hyper-extended; there is also a slight varus tendency in the feet; all these changes are more marked in the left foot. The hands present a slight degree

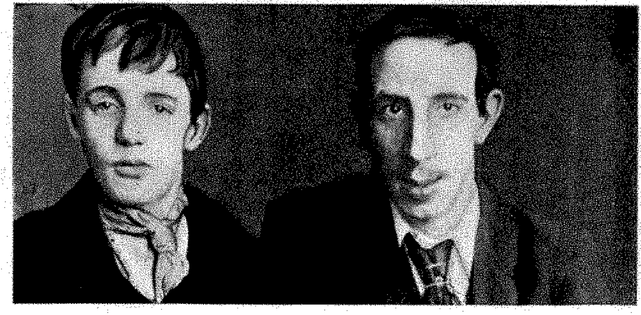


Fig. 1.

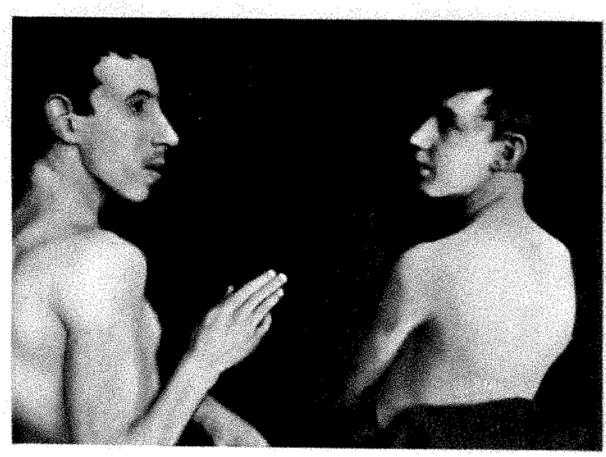


Fig. 2.

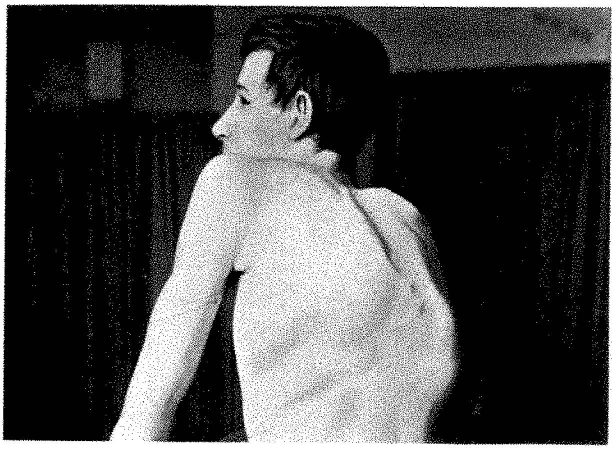


Fig. 3.

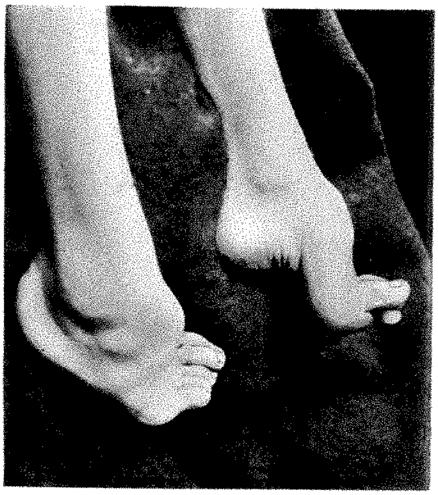


Fig. 4.

of the "main en griffe," the ring and little fingers being somewhat clawed (fig. 2). The metacarpus also appears too broad for the fingers.

Coordination. He is quite unable to assume or maintain the erect posture; he can get out of bed, cling to the side, and, reaching hold of neighbouring objects, guide himself about the room; he lifts his feet as if they were sticking to the ground at each step, and hobbles along. On attempting to stand alone, swaying movement of the body occurs, which would end in his falling backwards, if unsupported; this does not seem more marked when his eyes are shut; while sitting up in bed he is not steady. He is unable to thread a needle or perform other accurate movements of the hands, showing that ataxia is also present in the upper limbs.

Voluntary power appears to be normal in the arms, but is decidedly reduced in the legs, especially in flexion at the hip joint. The limbs are thin, but the muscles nowhere show any localised atrophy.

Reflexes.—Plantar reflexes are greatly exaggerated; knee-jerks could not at first be got when he lay in bed; but when sitting on the edge of the bed, with someone behind to lean against, they could be elicited on both sides; they were found to be somewhat of the spastic type, the whole of the limb going into a short spasm on tapping the tendon, and were more active on the left side.

Ankle clonus was obtained on the left side; three or four distinct contractions could always be produced. This point was confirmed by Dr. Kerr, and was constant whenever tested for; it is of great interest, as being a very unusual symptom, as also is retention of the knee-jerks, in Friedreich's ataxia.

Vaso-motor disturbance was evinced by the coldness of the extremities and the lividity of the hands.

Slight *nystagmus* occurred on wide lateral excursion of the eyes.

Speech was found to be characteristically affected, having a hesitating and peculiar careful plodding character, hastened at times, at the sacrifice of the end of a word.

Intelligence was above the average, and mentally he was very collected.

The following conditions were ascertained to be normal, viz.:—The pupils in size and reaction; the fundi; the perimetric tracings of the fields of vision; special senses; sensibility to touch, pain, and temperature everywhere; muscular sense; electrical reactions of muscles, the bladder and rectal functions. The other systems of the body were healthy.

Progress.—Under observation he improved a little, so that he could stand against the bed and take his coat off, and he could thread a needle. Plantar reflexes became normal instead of exaggerated: Pain was experienced several times in the shin of the right leg. Symptoms of thyroidism came on after nine days' treatment with tabloids; nux vomica was then given, and for the last three weeks he went through Roth's spinal exercises.

After leaving the Infirmary he remained in the same condition till November, 1898, when he says he had a severe attack of influenza, and has been quite helpless, having to be carried about and suffering great pain in the back and between the shoulders, that when he tries to stand he feels as if a very heavy weight were pressing on his feet. His handwriting is irregular, but has not changed much. His general health is fairly good.

(2) The second case is that of the youngest brother, Arthur R., aged 17, who came first under observation. He had come on account of a girdle sensation, following a wrestle with another lad ten days before.

History.—He had not been well for some years before this, for, when fourteen years old and growing fast, his back began to get curved, and has grown more so ever since. Two years later unsteadiness in the legs was first apparent, and has since then progressed; walking getting more and more uncertain. He has had no bladder or rectal troubles. The girdle sensation came on directly after a wrench to his back, from being thrown to the ground. It is situated about the ninth dorsal root zone, and goes away when he lies down.

On examination patient is not so tall as his brother, whom he does not resemble in peculiarity of features (fig. 1).

Deformity.—He has spinal curvature of the same kypho-scoliotic variety, but much less advanced; the convexity in his case is to the left in the dorsal region. The feet are long and narrow, but not deformed. In the right hand the little finger is somewhat clawed, and in both the metacarpus seems unduly broad.

Coordination.—There is an air of general unsteadiness about him, especially when agitated from self-consciousness; choreiform movements are also manifested, such as shrugging the shoulders, knitting and raising the eyebrows, and moving the scalp in an uneasy manner.

He has difficulty in maintaining the erect posture, but can balance himself after swaying to and fro, and apparently as well with his eyes shut as open.

In walking he lurches along, tacking from side to side to steady himself by catching hold of the furniture. The trunk is fairly steady when he sits up in bed. The head, however, is never still, owing to ataxia of the muscles of the neck; it appears to wander from its natural position, and has to be jerked back at times to be righted; there is marked hypertrophy of the sterno-cleido-mastoid muscles. The tongue cannot be held out steadily for any time. He is unable to thread a needle, the ataxia affecting also the arms.

Voluntary power is normal in the arms, but reduced in the legs; the limbs are spare, but the muscles firm, and show no localised atrophy.

Reflexes.—Plantar reflexes are extraordinarily active; a mere touch caused the leg to be thrown up off the bed and tickles him very much; especially active on the left side. Knee-jerks quite absent; ankle clonus absent; abdominal and epigastric reflexes brisk.

Slight *nystagmus* was produced on wide lateral movement of the eyes.

Speech is affected somewhat, being uncertain and wavering, though less laboured than his brother's.

Intelligence is above the average, and patient is of a nervous temperament.

Pupils were usually dilated, but reacted normally to light and accommodation. No hyperæsthetic zone corresponding to the girdle feeling could be found; nor any rigidity or tenderness of the spine.

The following points were found to be normal, viz.:—The fundi; perimetric tracing of fields of vision; special senses; sensibility to touch, pain, and temperature everywhere; muscular sense in judging weight; electrical reaction of muscles and the bladder and rectal functions.

The other systems of the body were unaffected.

Progress.—Under observation there was no great change, except that he learned to walk a little more steadily on the polished floors and to thread a needle. The state of the reflexes remained unchanged after full doses of nux vomica; latterly he performed Roth's exercises for spinal curvature. Nine months after he left he is reported to be about the same, except that his back is rather straighter. He occasionally experiences the girdle sensation.

REMARKS.

We thus see that, in the elder brother, the deformities of the back and feet, together with the ataxia, affection of speech, and nystagmus, presented a most characteristic picture, but the peculiarity was in the increase of myotatic irritability in the legs. While the younger had choreiform movements, ataxia, loss of knee-jerks, &c., but the skeletal deformities less marked. In both cases the left leg was more affected than the right. There were no ocular symptoms. The slight disturbances of sensation, viz., pains in the legs, transient anæsthesia in the thighs, and girdle sensation, may be noted, and, lastly, the fact that the ataxia did not appear until two years after the spinal curvature in both cases.

In the *Dublin Journal of Medical Science*, May, 1895, Mr. J. M. Nolan records "Three cases of Friedreich's Disease, associated with genetous Idiocy." In one of these there was ankle clonus and exaggerated knee-jerks; in the other two knee-jerks and ankle clonus were absent. I have seen a case similar to these myself, in a child six years old, mentally deficient from birth, who had marked ataxia, being hardly able to stand and had loss of knee-jerks; the pupil reactions were normal. A brother of this child had died a few years before, and was reported to have been idiotic and never able to walk.

Such cases as these may be allied to Friedreich's disease, but that term, I hold, belongs as yet to a definite body of symptoms and signs, as depicted by Friedreich, and found since to be strikingly constant.

But in these cases some of these classical features were absent, uncharacteristic symptoms, such as enlargement of the thyroid, were present, the mental condition was the reverse of what usually occurs, and the disease was congenital instead of appearing first in childhood or adolescence.

Still, they show, as do those I have detailed, that occasionally the lesion may be so distributed, as, in one case, to produce increase, and, in another, destruction of myotatic irritability among members of one family otherwise similarly affected.

ON CERTAIN RELATIONS OF THE CEREBRUM AND CEREBELLUM (ON RIGIDITY OF HEMIPLEGIA AND ON PARALYSIS AGITANS).

BY J. HUGHLINGS JACKSON, M.D., F.R.S.

As the subject of the relations of the cerebellum and the cerebrum to the spinal motor centres, and by them to the muscles, is—in consequence of Dr. Charlton Bastian's important researches on the effects of total transverse lesions of the supra-lumbar cord—now receiving considerable attention, I have asked permission of the Editor of BRAIN to republish in its pages two articles I wrote a little more than twenty years (1877 and 1878) ago, one on "Rigidity in Hemiplegia," and one on "Paralysis Agitans" (Parkinson's Disease).

REMARKS ON RIGIDITY[1] OF HEMIPLEGIA.

(*The Medical Examiner*, April 5, 1877.)

With reference to several cases of hemiplegia, Dr. Hughlings Jackson expressed the opinion that the rigidity in hemiplegia is not owing to the cerebral lesion nor to the lateral sclerosis. There is evidently a duplex symptomatic condition, negative and positive; with loss of power over the muscles there is tonic action of them. Whilst the primary cerebral lesion can account for the paralytic element—the negative condition—it cannot (nor can the sclerosis in the lateral column) account for the tonic condition of the muscles, the positive element. Negative states of the nervous centres cannot *cause* positive states of muscles, they may *permit* them. His speculation is that the rigidity is owing to unantagonised influence of the cerebellum. He believes that in health the whole of the muscles of the body are doubly innervated—innervated both by the cerebrum and cerebellum; there being a co-operation of antagonism betwixt the two great centres. Whilst the cerebrum innervates the muscles in the order of their action from the most voluntary movements (limbs) to the most automatic (trunk), the cerebellum innervates them in the opposite order. This also is supposed to be the order of their degree of influence on parts; and is equivalent to saying that the cerebellum is the centre for continuous movements and the cerebrum for changing movements. Borrowing medical terms to describe normal physiological conditions, the former are tonic the latter clonic. The muscles which on the above suggestions, are chiefly innervated by the cerebellum, are those which have the fewest different, the most tonic, the most "confluent" movements; the reverse for those which the cerebrum chiefly innervates. Thus, in walking, the cerebellum preserves the equilibrium of the body, tends to "stiffen" all the muscles; the changing movements of walking are the result of cerebral discharges overcoming in a particular and orderly way the otherwise continuous cerebellar influence. This is what is meant by a "co-operation of antagonism." The cerebrum does most "work," the cerebellum does little (if any) "work"; from continuous action of muscles balancing one another there is dissipation of energy (heat); from cerebral action there are molar movements (work).

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[1] 1899. In some cases of hemiplegia there is a kind of pseudo-rigidity; I mean a rigidity from joint disease ("locking of the joints"), with no or very little muscular rigidity. I think this pseudo-rigidity occurs far oftener with left than with right hemiplegia.

When, however, the influence of the cerebrum is permanently taken off by disease of the cerebrum, as in hemiplegia, from the parts which it most specially governs [arm and leg], the cerebellar influence is no longer antagonised; there is unimpeded cerebellar influx and hence rigidity of the muscles which in health the cerebrum chiefly innervates. The principle, he thinks, accounts for the duplex, negative and positive, conditions in the contractures of hemiplegic children, in the athetosis of Hammond, and accounts for the rigidity and "propulsive" walk in paralysis agitans; temporary removal of cerebral influx also for tetany and certain hysterical attacks, and also for some post-epileptic conditions of movements. Physiological experiments were adduced in favour of the doctrine that two impulses arriving at a centre interfere with one another; the opposite effects of ligature in epileptiform seizures and in tetany were spoken of.

The above hypothesis is, Dr. Hughlings Jackson considers, only an application on a large scale of Thompson Dickson's[1]

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[1] 1899. The "Principle of Loss of Control" was, I believe, first stated by Bernard and afterwards by Anstie, and then by Thompson Dickson.

Principle of Loss of Control, a principle applicable to all nervous centres, as is, Dr. Jackson thinks, the physiological Principle of Antagonism. In healthy operations the two principles are displayed; did not centres "resist" one another there could be no independence of operations; differentiation would be practically anulled. On the other hand, if some centres could not overcome the resistance of others—discharge them by their discharges—there would be no association of operations, differentiation would be useless; and if there were not some order of "resistances" and of "dischargeabilities" there would be no orderly co-operation.

ON CEREBRAL PARESIS OR PARALYSIS, WITH CEREBELLAR TREMOR OR RIGIDITY.

(*The Medical Examiner*, March 28, 1898.)

In the *Examiner*, April 5, 1877, are reported some remarks by me on the interpretation of the rigidity in hemiplegia. I then suggested that the condition is duplex, that there is a negative condition, "cerebral paralysis," due to the destructive lesion in the corpus striatum, and a positive condition "cerebellar rigidity," due to increased cerebellar influx. The hypothesis starts with the assumption that the spinal centres receive impulses from both the cerebrum and cerebellum, which impulses in health interfere with one another (inhibit one another). If so, we should not say that the cerebral lesion, nor the wasting in certain spinal tracts consecutive upon it, *causes* rigidity; negative lesions can only cause negative conditions in muscles; in this case the paralysis. But on the hypothesis the cerebral lesion, in other words, loss of cerebral influence on the spinal centres, may *permit* the rigidity, for then the cerebellar influence is no longer interfered with, and, metaphorically speaking, "flows into the parts deserted by the cerebral influence." Hence it is better to say "unantagonised cerebellar influx" than "increased cerebellar influx." The cerebellum is healthy, or if over-active in effect,[1] it is not so because its cells have become morbidly over-unstable, but because there is less or no resistance to overcome, or, as we say, less or no cerebral influence to antagonise.

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[1] 1899. I have been supposed to hold that there is disease of the cerebellum in cases of paralysis agitans. On the contrary, as will be seen later in the text, my hypothesis implies that in this malady there is integrity of the cerebellum; the tremor and rigidity of paralysis agitans are, I suppose, the outcome of activities of perfectly healthy structures, cerebellum and anterior horns.

I do not believe that any *continuous* and *positive persisting* symptoms—positive symptoms so continuous and *persistent* as the tremor and rigidity of paralysis agitans—are ever the *direct* result of disease—of disease in the proper sense of pathological process. I think that, like those of paralysis agitans, they are always the *indirect* result of disease, and that they are directly the result of activity or of over-activity of healthy structures, that they are problems in the domain of physiology, not of pathology.

Mutatis mutandis, the same explanation applies to rigidity of the spinal and other muscles in cases of destroying lesions of the middle lobe of the cerebellum; there is then " cerebellar paralysis " and " cerebral rigidity."

I wish now to show how the hypothesis applies to the interpretation of several symptoms of paralysis agitans.

The regional distribution of this motor affection points unmistakably to the cerebrum (whether of the motor tract or cerebrum proper is not said) as the seat of the morbid anatomy. It is essentially hemiplegic, although very commonly it *becomes* two-sided. I believe that we have here, too, a minus cerebral and a plus cerebellar condition. It is sometimes asserted that there is no paralysis in what is called *paralysis* agitans; but some of those who say so add that the movements are slow, and slowness of grasp is as much evidence of paralysis as weak grasp is. To ignore the element of rapidity in estimating the " momentum " of a mobile part would be like ignoring the velocity of a cannon-ball in estimating its momentum. It is certain that we have tremor and rigidity.[1]

On the supposition that the cerebral influence is diminished, we may explain the tremor—negative clonic cerebral spasm (most of the spasm in ordinary epileptiform seizures being positive clonic cerebral spasm). On the supposition that the cerebral influence is taken away altogether, we may explain the rigidity. Tremor, at least rhythmical tremor, is a minor degree of tonic spasm. If, experimentally, shocks at comparatively long intervals are sent into a muscle, there is a sequence of contractions, the analogue of tremor; but if they be sent in at exceedingly short intervals, there is tetanic contraction, the analogue of rigidity. Thus the tremor of paralysis agitans differs from the rigidity of hemiplegia, not fundamentally, but in degree; in the former the cerebral influx is diminished; in the latter it is taken off altogether. And as the disease progresses, or, as the hypothesis has it, when the cerebral influx ceases entirely, then rigidity of the parts *does* ensue, which in tremor were approaching rigidity.

(1) In health the cerebellar influx is fully antagonised; in (2) the early stages of paralysis agitans it is intermittently antagonised—the movement constituting each single tremor occurring

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[1] In a few cases there is no tremor, or scarcely any; there is rigidity only.

betwixt the cerebral impulses; in (3) late stages it is not antagonised at all, and there is such a stream of cerebellar impulses that rigidity occurs. We have cerebral paresis with cerebellar tremor; later, cerebral paralysis with cerebellar rigidity.

So much for the parts which the cerebrum *chiefly* innervates in health, and which it slowly "abandons," and which, in consequence, the cerebellar influx gradually "invades."

In paralysis agitans there is "loss of expression" of the face, but this so-called "loss" of expression of the face is one *fixed* (starched) expression. An unvarying expression, however caused, is in effect a loss of expression. The hypothesis is that there is some facial paralysis "caused" by the cerebral disease, and some facial rigidity, owing to "permitted cerebellar influx."

On the hypothesis (see *Examiner*, April 5, 1877) the spinal muscles are those which the cerebrum influences least and the cerebellum most; thus there is rigidity without prior tremor. This is manifested by the well-known attitude, and indirectly by the propulsive gait. The rigid state called "attitude" of the body, face, and limbs is more characteristic of the disease than the tremor, in spite of the name "paralysis agitans."

This is a mere outline.[1] It may be remarked that the general attitude often seen in cases of paralysis agitans (face, arms, and legs) is like that seen in cases of rapid locomotion; it is at least a good caricature of the position, supposing locomotion to be suddenly arrested, and parts of the body remaining fixed. In running, the body is bent forward, the arms are flexed, &c., and the facial muscles come into vigorous action.[2]

As before said (*op. cit.*) the hypothesis is applied to cases of athetosis, and to the mixed condition of paralysis with twisting movements in persons hemiplegic from early life.

For *all* morbid over-mobile conditions of one side I have suggested the name hemikinesis, although I have been supposed to use it only for the athetosis of Hammond. But we have two different sub-classes; the hemikinesis due to cerebral discharges (unilateral chorea and unilateral epileptiform seizures), and the hemikinesis owing negatively to cerebral destroying lesions with (positively) permitted cerebellar influx.

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[1] With the assistance of my clinical clerk, Mr. Whitford, I tried, a few days ago, the effects of ligature on a patient, the subject of paralysis agitans, the tremor being on both sides. At first trials we obtained arrest of the tremor of the arms, even when the ligature was applied round one calf, but at the second *séance* we got no such results. The plan is worthy of trial in slighter cases.

[2] 1899. The attitude in an advanced case of paralysis agitans is something like that of a feeble old man when he is going upstairs.

REMARKS, 1899.

I have written on this subject several times since 1878. (*Med. Times and Gazette*, February 12, 1881; BRAIN, January, 1888, p. 312 *et seq.*; *Brit. Med. Journal*, March 5, 1892; *Lancet*, December 12, 1896, and January 8, 1898.) In these papers I have acknowledged all the difficulties I knew of.

To the hypothesis propounded in the two papers reproduced from the *Medical Examiner*, it was objected that the "fact" that upon complete transverse lesion of the cord above the lumbar enlargement (whereby both cerebral and cerebellar influences are cut off from motor centres below that transverse lesion) the knee-jerks are exalted and that the legs are, or soon become, rigid—that these super-positive conditions exist when the cerebellum is altogether excluded—disprove the hypothesis.

I was so impressed by this "fact," as I then took it to be, that[1] I went a long way towards abandoning the doctrine of cerebellar influx, if not all the way. I then wrote: "I admit . . . that since after section of the cord right across, destroying communication with both cerebrum and cerebellum, there is increased reflex activity of the parts below, we cannot suppose that unantagonised cerebellar influx is essential for the conditions mentioned. I make this admission in consequence of some verbal criticisms by Ferrier."

Since I wrote that, Dr. Charlton Bastian (Quain's "Dictionary of Medicine," p. 1480 (1882), "Paralyses, Cerebral, Bulbar and Spinal," 1886,[2] and also "On the Symptomatology of Total Transverse Lesions of the Cord," *Med. Chir. Trans.*, 1890), has done far more important work on the matter than I have. He has shown that upon a complete transverse lesion of the cord above the lumbar enlargement there is, contrary to what, heretofore, had been universal physiological and medical doctrine, flaccidity of the legs and loss of the knee-jerks.

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[1] "On a case of Temporary Left Hemiplegia with Foot Clonus and Exaggerated Knee Phenomenon, after an Epileptiform Seizure beginning in the Left Foot," *Medical Times and Gazette*, Feb. 12, 1881.

[2] In this work, "Paralyses, &c.," 1886, p. 538, Bastian writes, ". . . with *a total transverse* lesion in the lower cervical region, nearly all reflexes dependent upon lower portions of the cord are *abolished rather than exaggerated.*"

Bowlby (*Med. Chir. Trans.*, 1890), Thorburn (*Med. Chronicle*, May, 1890), and Bruns, of Hanover (*Archiv fur Psychiatrie*, Band xxv., pp. 1-72), have confirmed Bastian's conclusions.[1] I do not imply that the writers just mentioned accept my hypothesis of the nature of the dynamical relations of the cerebrum and cerebellum. My hypothesis is rejected by Bruns, also by Gerhardt, and by Ferrier and other eminent neurologists.

Dr. Charlton Bastian's conclusions as to the state of the muscles and tendon reactions of parts below a *complete* supra-lumbar transverse lesion of the cord, are now admitted by nearly all medical neurologists to be correct.[2] The real "facts" of cases of the complete transverse lesions mentioned are not against the hypothesis I put forward in 1877-8. Bastian wrote (*Med. Chir. Trans.*, vol. lxxiii., 1890, p. 208) :—"I came to the conclusion that a notion closely akin to that of Dr. Hughlings Jackson was most capable of explaining all the facts." After considering the then (1890) current views as to the causation of rigidity and exaggerated tendon reactions in hemiplegia, Bastian wrote (p. 209) :—"Great difficulties formerly stood in the way of explaining many of the facts without the aid of some such views (although grave objections could always be alleged against them); hence the few adherents which the counter-explanation of Dr. Hughlings Jackson has hitherto been able to command. Now, however, it seems to me that the new facts established in this paper will be found to be altogether opposed to the fashionable views above cited, and to be just as much in favour of some modification of the doctrine of Hughlings Jackson."

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[1] See a most able paper, "On the Conditions of the Reflexes in Total Transverse Division of the Spinal Cord," by Ernest S. Reynolds, BRAIN, vol. xviii., p. 148 *et seq.*, 1895.

[2] Sherrington writes in a very remarkable and most valuable paper (*Trans. Royal Society*, vol. cxc., B, 1898, pp. 144-145) :—"My results on Monkeys bear out strikingly and fully what Bastian describes as the typical condition in Man after complete transverse destruction across the cord. The chief difference is that in the Monkey in most cases—partly, perhaps, because the lesion is more localised by experimental infliction than by accidental—the depression is not so severe. For instance, the knee-jerk, which disappears almost immediately after the transection, returns usually in a week or ten days (Sherrington, *Journ. of Physiol.*, 13, 1892; A. S. F. Grunbaum, *Journ. of Physiol.*, 16, p. 368); often, however, not for three weeks; occasionally, on the other hand, in ten minutes."

In the second reprint (*Medical Examiner*, 1878) I spoke of localisation of the disease in paralysis agitans, suggesting that the regional distribution of this motor affection points to the cerebrum. I have, since 1878, submitted the hypothesis that in this malady there is slowly-spreading atrophy of cells of the Rolandic region of the cortex in the order of their size, from smallest towards largest. Presumably these cells, in their order from smallest to largest, represent muscles,[1] in their order from smallest towards largest. In paralysis agitans the interossei[2] are the muscles of the hand which are preponderatingly affected, and the set of the hand resembles that of the tetany of children. In most cases of ordinary hemiplegia with rigidity there is destruction of fibres of some part of the course of the pyramidal tract (internal capsule), a comparatively random and brutal lesion (clot or local softening). In most cases of this hemiplegia with rigidity the set of the hand is not interosseal, but is due especially to contraction of the large flexors and extensors; this set of the hand a little resembles that of the hand in carpo-pedal contractions of children. I believe that both tetany and carpo-pedal contractions are owing to loss of cerebral control permitting greater cerebellar influx, and surmise that, in children, the differences in the disposition of the thumbs and fingers and of the hands in carpo-pedal contractions and tetany, depend, at least partly, on differences in the degree of development (or of perfection) of the pyramidal tract and cortex; the nervous arrangements for the intrinsic muscles will, I imagine, be later in their development or perfection than those for the large flexors and extensors of the hand.

A case, very important in many ways, has been published by Strümpel (*Deutsche Zeitschr. f. Nervenheilk.*, B. v., 1894) of a woman whose attitude was very like that of a subject of advanced paralysis agitans. Brissaud (*Leçons sur les Maladies Nerveuses*,

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[1] Properly "small and large movements." See my second Lumleian Lecture, *Brit Med. Journ.*, vol. i., 1890. For important remarks on the significance of sizes of nerve-cells see Bevan Lewis "On Mental Diseases," 2nd ed., 1899.

[2] In some cases of paralysis agitans there is over-contraction of the interossei, and thus hyper-flexion of the first phalanges and hyper-extension of the other phalanges of the fingers. See a very interesting paper, *Des Déformations de la Main*, by J. E. Siotis. I need scarcely remind the reader of Charcot's important researches on paralysis agitans, in which, among many other things, he considers the set of the hands in cases of paralysis agitans, likening the disposition of the fingers in some cases to that in some cases of chronic arthritis.

Salpêtrière, 1893-4) reproduces (p. 45 *op. cit.*) a portrait of this patient, and (p. 486 *op. cit.*) says of it :—" Est-il possible d'imaginer une attitude et une physionomie plus *parkinsoniennes ?* C'était une pseudo-bulbaire, puisqu'elle avait le syndrome d'une paralysie labio-glosso-laryngée spasmodique, causée par une double lesion systematique du faisceau paramidal." (See also Brissaud, *op. cit.*, pp. 41 *et seq.*) There was no tremor ; there was rigidity of face, tongue, neck, arms and legs. There was difficulty in turning the eyes to the left, and ultimately all ocular movements were lost. Strümpell writes (*op. cit.*) :—" On being asked, the patient is unable to carry out the smallest movement in any part of the body or with the eyes. But of her own accord she occasionally makes a slight movement with the eyes or with the eyelids." No morbid changes were found in the cells of the cortex cerebri. Degeneration was traced upwards beyond the upper end of the internal capsule, but could not be followed to the cortex cerebri. The lesion in Strumpel's patient was a slowly-developed one, whereby cerebral control would be slowly taken off anterior horns, and consequently, as I suppose, there would be permitted gradually greater cerebellar influx on those parts (anterior horns) from which the cerebrum was being, by the lateral sclerosis, slowly cut off. I do not say that this case was one of paralysis agitans, but I think it illustrates, if it does not confirm, the *principle* of the hypothesis I have put forward as to the pathology and physiology of that malady.

In cases of paralysis agitans, as in so many other nervous maladies, we have to bear well in mind Broadbent's hypothesis,[1] 1866. Bearing it in mind, I should say that double hemiplegia is more than the double of hemiplegia. In hemiplegia the bilaterally-acting muscles of both sides escape, or suffer very slightly, whereas in double hemiplegia the bilaterally-acting muscles of both sides suffer as well as do the unilaterally-acting muscles of both sides. Hence, in Strümpel's patient (symptomatically a case of double hemiplegia with rigidity), there was, as Brissaud puts it, pseudo-bulbar paralysis ; there was involvement of very important bilaterally-acting muscles of both sides.

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[1] I have profited very greatly by the application of Broadbent's hypothesis to the explanation of complex neurological problems. Thirty years ago (*Med. Times and Gazette*, Aug. 15, 1868) I wrote, under the heading "Remarks on Broadbent's Hypothesis," to urge those who observe defective bilateral movements with hemiplegia—particularly difficulty in swallowing—to enquire carefully if the patient has not been previously paralysed on the other side. Again, at an autopsy on a patient known to have been paralysed of *but one side*, and who had had difficulty in swallowing, we should search both sides of the brain for evidences of disease.

An advanced case of paralysis agitans *is* double hemiplegia with rigidity (and some tremor, which is an approach to rigidity). It will be found in some cases of this malady that, if there be not bulbar (pseudo) paralysis, there is involvement of other bilaterally-acting or alternately-acting muscles—rigidity of those of the face, neck, back, and abdominal wall. The hypothesis may be considered from another standpoint.

In an early stage of etherisation for surgical purposes there is muscular rigidity, and the knee-jerks are exalted. I think it possible that this occurs when the small cells of the cerebral cortex have succumbed to the ether, and when the large cells of the cerebellum have not been rendered functionless by it. In this stage, according to my hypothesis, there is negatively loss of some degree of cerebral control, and positively there is permission of a greater degree of cerebellar influx. In later stages, when I suppose the large cerebellar cells also have been rendered functionless, there is flaccidity of muscles and loss of the knee-jerks.

The situation, however, is complicated. The ether has, so to say, no malice against any particular part of the nervous system, but will put *hors de combat* small nerve-cells, wherever they are (cerebral, spinal, or cerebellar), sooner than it will large cells, wherever they are.

Dr. Hewitt, in his remarkably interesting work, "Anæsthetics and their Mode of Administration," p. 154, says of etherisation:—"In exceptional cases a fine tremor, known as 'ether tremor,' may occur." Perhaps the annulling of function of cells of the cortex is not solely by ether or chloroform, but both by the anæsthetic used and by supervenous blood (deficiency of oxygen). I say this in consequence of what Dr. Hewitt writes, p. 281 *op. cit.*:—"Rigidity will often disappear when more air is allowed with the anæsthetic, a fact which leads one to suppose that the condition may sometimes depend upon intercurrent asphyxiation." If so, there may be removal of cerebral control, partly by the action of the anæsthetic and partly by that of supervenous blood. But there is a difficulty to my hypothesis, so far as supervenosity is concerned. Risien Russell has found that the knee-jerks in dogs are exaggerated in early stages of artificial asphyxia, even when the supra-lumbar cord has been divided. It may be that in rigidity under anæsthetics, &c., super-venous blood, which annuls the function of cortical cells (of the Rolandic region at least) and which stimulates some medulla centres (respiratory, &c.), may stimulate some of the cells of anterior horns, and thus produce the rigidity or part of it.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

AT a Pathological Meeting held on Thursday, December 7, 1899, at 11, Chandos Street, W., the following communications were made :—

(I.) Dr. F. E. BATTEN and Dr. J. S. COLLIER.—*Spinal cord changes in cases of cerebral tumour.*

The object of the paper was to show that degeneration of the posterior columns of the cord frequently occurs in cases of cerebral tumour. The authors have examined twenty-nine cases of cerebral tumour occurring in patients of all ages and in varying situations, and they find that degeneration of the posterior columns to a greater or lesser degree occurs in about 65 per cent. of the cases. A short abstract from the papers of previous observers was then given, and the suggested explanation of the changes found discussed. Of these, the most important were (1) a toxic process; (2) increased intra-cranial pressure; (3) venous stasis, anæmia, or thrombosis; (4) retrograde degeneration.

The character of the degeneration was such that though readily shown by the Marchi method it was not obvious by the Weigert-Pal method. The degeneration affects the posterior columns of the cord, and more especially the postero-external columns in the lower cervical region, but in certain cases the degeneration affects the lumbar and even the sacral region of the cord. The degeneration can be traced up to the posterior column nuclei. The degeneration is of root origin, as shown by certain cases where only a few roots are affected; the degeneration is limited to this root area, and also by the fact that the endogenous tracts of the cord tend to escape, although it cannot be said that they are perfectly free from degeneration. (Few will deny, however, that these endogenous tracts also contain fibres of exogenous origin.)

The posterior nerve roots usually show some degeneration, but always considerably less than the degeneration in the cord, and they may in some cases show none.

The posterior root ganglia appear perfectly normal.

The degeneration neither depends on the situation of the tumour nor on the nature of the growth, but it is dependent on the increase of intra-cranial pressure. An increase of the intra-cranial pressure tends to distend the sub-arachnoid space in the spinal cord, and such distension puts traction on the posterior nerve roots. It has been shown by other observers that the posterior nerve root is especially thin and constricted at the point where it enters the spinal cord. Traction would therefore tend to injure the roots especially at this point. It is therefore argued that the degeneration in the cord is an ascending degeneration, while that in the posterior roots is a retrograde change. Such a view is borne out by the present series of cases, since, while there is marked degeneration in the posterior columns of the cord, littl or no degeneration can be seen in the posterior roots.

Certain clinical features were next dealt with, viz., the effect of operation, the condition of the knee and arm-jerks, and the presence of optic neuritis.

The following conclusions were arrived at :—(1) That degeneration of the posterior columns of the spinal cord frequently occurs in cases of cerebral tumour, *i.e.*, about 65 per cent.; (2) that such degeneration is more liable to affect the spinal cord in the cervical region than in the dorsal or lumbar, and is more marked in the postero-external than in the postero-internal columns; (3) that such degeneration is of root origin, and arises from the point where the root enters the spinal cord, the posterior roots being always less affected than the posterior columns and may show no degeneration; (4) that such degeneration is due to traction on the posterior roots by the distension of the spinal arachnoid owing to the increased intra-cranial pressure; (5) that such degeneration is independent both of the situation and of the nature of the tumour except in so far as their liability to give rise to the preceding condition is concerned; (6) that optic neuritis bears no relation to the occurrence of posterior degeneration; (7) that the absence of the knee-jerk (except in the semi-comatose state) indicates posterior degeneration, but that their presence does not negative such a condition; and the absence of the arm-jerks probably has the same significance.

(II.) Dr. WILFRID HARRIS.—*An experimental investigation on the decussation of the optic nerves in various animals, and on the path of the reflex for the contraction of the pupil to light (Meynert's fibres).*

This work was undertaken as a necessary preliminary to the study of reflex iridoplegia in man, or the Argyll-Robertson pupil. Clinical study of the consensual reflex contraction of the pupil in cases showing uni-ocular Argyll-Robertson pupil prove that the usually accepted path for the light fibres from the corpus quadrigeminum to the third nucleus of the same side (the two nuclei being connected together), will not explain the results obtained ; inasmuch if light be directed obliquely upon the temporal half only of the retina of the affected eye, then the impulses travel up only by the optic tract of that side, owing to the non-decussation of the optic fibres from the outer halves of the retina in man. In such case the pupil of the affected eye does not contract to light, whereas there is brisk consensual contraction of the opposite pupil. According to the accepted scheme this could only result through the impulses passing through the sclerosed Meynert's fibres or affected third nucleus of the damaged side, which is entirely improbable.

Now in the lower animals, fishes, amphibia, birds, and lower mammals, the optic nerves decussate completely, as shown by sections of chiasma of toad, chameleon, pigeon, owl, and rabbit. Studies of the pupil reflex to light in the toad, frog, pigeon, parrot, owl and rabbit, show that only the pupil on which light is thrown contracts reflexly. There is no consensual reflex to light in these animals. Therefore, since there is total decussation at the chiasma there must exist in addition a posterior total decussation for the pupil-reflex fibres between the optic lobes and third nuclei. This then is probably the primitive arrangement in animals without binocular vision.

Partial binocular vision however is obtained in warm-blooded carnivorous animals, which require especially keen sight to follow up their prey, as seen in hawks and owls, and amongst mammals especially in the cat tribe. Yet the decussation remains complete in all birds, as proved by sections of chiasmata in owls, and by degeneration following enucleation and Marchi staining in pigeons ; and in these only the pupil on which light is thrown will contract reflexly. Partial decussation is seen first in mammals. Practically complete in rabbit, with no binocular vision and unilateral pupil reaction, only a very few fibres passing up the optic tract of the same side; in the cat, with good binocular vision and consensual pupil reaction, degeneration results show apparently an equal number of degenerated fibres passing up the tracts of each side. Wounds of the optic tract and corpus quadrigeminum on one side in cats have produced hemianopia with hemianopic pupil reaction, and marked degeneration in Meynert's fibres, which decussate ventrally at level of third nuclei to form a tract ventral to the opposite posterior longitudinal bundle, with some degenerated uncrossed fibres in the posterior longitudinal bundle of the same side. These fibrès are precisely similar to the degenerated fibres in Meynert's decussation in cats shown by Boyce after extirpating one hemisphere.

None of these fibres can be traced either into the third nuclei or third nerves. But in animals with semi-decussation at the chiasma and consensual pupil reflex the primitive posterior total decussation of the pupil-reflex fibres must either be modified so that the corpus quadrigeminum of one side is connected with the third nucleus of the same as well as the opposite side, or else the two third nuclei must be tied together so as to react consensually. And in birds it is evident that the third nuclei are not connected together as regards the light reflex, and in man the phenomena of uniocular Argyll-Robertson pupil already spoken of negative the possibility of any connection between the nuclei being the path for the consensual light reflex. Therefore the former arrangement, or posterior semi-decussation, analogous to the semi-decussation at the chiasma is theoretically the necessary path for the light reflex in cat and the higher mammals. Such a path is probably furnished by the semi-decussation of Meynert's fibres as shown by the degeneration experiments in cats; and the probable path of the light reflex is then as will be shown in a diagram.

(III.) Dr. MOTT and Mr. A. F. TREDGOLD.—*Hematrophy of the brain and its effects upon the cerebellum and spinal cord.*

Clinical.

J. E., male, aged 26, single; occupation, shoe-black. Considered to be a case of epilepsy with dementia. He has frequent fits, and has had them since childhood. He is very considerably demented, but subject to occasional sudden attacks of maniacal excitement. There is paralysis of the right arm and leg, with increased reflexes. Pupils are equal and react to light and accommodation. He died at the age of 30 of acute phthisis.

Post-mortem examination.

Skull.—The left side is much thicker than the right (in some places twice as thick), although there is no asymmetry when viewed from the outside.

Brain.—Marked wasting with enormous dilatation of ventricle of the left hemisphere, which weighs less than a third that of the right.

Cerebellum.—Atrophy of the right upper quadrant.

Spinal cord.—Notably asymmetrical, due to wasting of antero-lateral columns on left side.

Microscopical examination.

Brain (left hemisphere).—Great atrophy of basal ganglia, chiefly affecting the optic thalamus. Cortex as a whole considerably thinned; there is an absence of large pyramidal cells, and the polymorphous cells appear to be slightly deficient. The smaller pyramids do not seem to be affected. There is a very great diminution in the number of nerve fibres; most notably is this the case with those of the projective system. The commissural and association fibres are not nearly so much affected.

Cerebellum.—Here the atrophy is confined to the lobus culminis of the right upper hemisphere; the layer of large granule cells lying immediately underneath the cells of Purkinje are not diminished, and the interlacing (? association) fibres are not affected. There is an entire absence of the cells of Purkinje, and a very great diminution of the coarse bundles of fibres forming the rays. The right superior peduncle is but a quarter the size of the opposite side. In the *pons* and *medulla* there is great diminution in the fibres of the fillet and pyramidal tracts on the left side. The olives and restiform bodies are symmetrical. The posterior column nuclei and arciform fibres have not yet been examined.

Spinal cord is obviously asymmetrical to the naked eye, there being marked atrophy of the left side all the way down the cord as far as L. 1 segment, and the atrophy being especially pronounced in the antero-lateral columns.

The following is a brief summary of the changes found in the different tracts of the cord when examined microscopically.

Left direct pyramidal.—Some sclerosis extending down as far as the first dorsal segment. *Right crossed pyramidal* is sclerosed and contains many swollen fibres as far down as L. 4. *Antero-lateral* descending tracts on left side are markedly deficient as compared with the opposite side. This condition can be seen as far as L. 3. There is some slight sclerosis at the periphery of the cord in the cervical region, but the chief condition in these columns is not one of sclerosis, but of deficiency—the tracts do not seem to be present at all. It is the absence of these tracts which gives rise to the marked asymmetrical appearance of the cord. The *direct cerebellar tracts* are normal. In the cervical region there is sclerosis in Goll's column, the left side being slightly more affected than the right. The spinal ganglia were examined by Nissl's method, but showed no change. *Burdach's columns* are healthy. *Cells of anterior horns.*—There is a marked diminution in the cells of the right side; indeed, it can readily be seen by the naked eye that the right anterior horn is atrophied. Sections stained by Nissl also show that many of the cells which are present are undergoing degenerative changes. It must be said, however, that this diminution of nerve cells appears to be confined to the cervical and lumbar regions. No notable difference can be detected between the two horns in the dorsal region. In the cervical and lumbar regions, whilst there is a general numerical diminution of cells on the right side as compared with the left, it does certainly appear that this diminution is most marked in those cells forming the lateral groups and those at the base of the horn, and this is especially so in the 8 C., 4 and 5 L., and 1 S. segments. In the affected horns the nerve fibres are also deficient.

Clarke's column.—In the 12 D. and 1 L. segments there are certainly fewer cells on the right side, but above this the two sides are quite symmetrical, and all the cells appear particularly healthy.

Rules

AND

LIST OF OFFICE BEARERS AND MEMBERS

OF THE

Neurological Society of London,

1899,

WITH THE

Annual Report of Council, and Balance Sheet for the Year 1898.

LONDON:
JOHN BALE, SONS & DANIELSSON, LTD.,
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1899.

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Secretaries.

J. S. RISIEN RUSSELL, M.D., F.R.C.P.
W. S. COLMAN, M.D., F.R.C.P.

Neurological Society of London.

REPORT OF COUNCIL.

FEBRUARY 2, 1899.

The Council has much pleasure in reporting the continued success and prosperity of the Society. The members now number 206.

The Inaugural Address was delivered at the Annual General Meeting on January 13, 1898, by Mr. Victor Horsley, F.R.S., on "The Degree of Discharge of Different Nerve Centres."

The vacancy caused on the list of Honorary Members by the death of Professor Du Bois Reymond, of Berlin, has been filled by the election of Professor Hitzig, of Halle, formerly one of the Corresponding Members of the Society, and the vacancy thus caused on the list of Corresponding Members has been filled by the election of Professor Gustaf Retzius, of Stockholm.

A feature in the year's programme has been a visit, in April, to Cambridge, where, at the invitation of the Vice-Chancellor of the University, Dr. Alex. Hill, formerly President of the Society, a Physiological Meeting was held. At the conclusion of the meeting the Society was most hospitably entertained by the Vice-Chancellor. This was the first occasion on which the Society has met out of London.

As during last year, the Proceedings have been published at greater length in "Brain" than was the custom in former years, and an abstract appended to this Report gives some idea of the value and character of the work of the Society during the past year.

The Council reports with regret the resignation of the Senior Secretary, Dr. Frederick Mott, after four years of valuable service rendered to the Society.

Proceedings of the Society during the year 1898.

January 18th, Mr. Victor Horsley, F.R.S., Inaugural address, "The Degree of Discharge of Different Nerve Centres," *Brain*, vol. xxi., part lxxxiv.

February 24th, Dr. Donkin (1) "Spastic Paraplegia in a Child aged 4 years;" (2) "Functional Hemiplegia with Hemianæsthesia in a Man aged about 50 years;" (3) "A Case of Paralysis Agitans." Dr. Mott, "A Case resembling Scleroderma in which there was Diminished Sensibility over the Area supplied by the Two Inferior Divisions of the Fifth Cranial Nerve, with loss of taste over the anterior two-thirds of the tongue, and loss of smell." Dr. Herbert Hawkins, "Case of Peroneal Type of Muscular Atrophy." Dr. Beevor, "Case of Syphilitic Spinal Meningitis." Dr. Leonard Guthrie, "Case of Unilateral Syringo-myelia with Bulbar Symptoms." Dr. Stephen Mackenzie, "A Case of Nodding Spasms." Dr. Ormerod, "A Case of General Athetosis." Dr. F. E. Batten, "Friedreich's Disease with Mental Defect." Dr. Aldren Turner, "A Case of Diplegia Facialis, with paralysis of both external recti, defect in finer movements of hands, spastic gait and double club-foot."

April 23rd, Dr. Alex. Hill, "Some Specimens of Granules." Professor Macalister, "The Race-Characters of Australian Brains." Dr Langley, "Some Points relating to the Sympathetic System." Dr. Gaskell for Miss Alcock, "The Distribution of the Facial Nerve in Ammocœtes." Dr. F. E. Batten (1) "Nerve Terminations in Muscle Spindles;" (2) for Dr. Sihler, of Ohio, "Motor Nerve Termination within the Muscle Spindle." Dr. Mott, "Degeneration of the Neuron."

June 30th, Dr. C. E. Beevor opened a discussion on "The Accurate Localisation of Intra-cranial Tumours," and Drs. Byrom Bramwell, Michell Clarke, and Sharkey took part in the discussion.

October 27th, Drs. Ormerod and F. E. Batten, "Idiopathic Muscular Atrophy (Landouzy-Déjérine type) in Mother and Son." Dr. Beevor, "Unilateral Wasting and Paralysis of the Lower Half of the Trapezius." Dr. Sinigar, "Case of Idiopathic Muscular Atrophy." Dr. F. W. Mott, "Arsenical Neuritis from Local Action of the Poison followed by general Degenerative Effects upon the Nervous System." Dr. Ormerod, "A Case of Hereditary Chorea." Dr. Lunn and Mr. Ballance, "Case of Removal of Cerebellar Tumour, three years and eleven months after the operation" (case shown at a meeting of the Society eighteen months ago). Mr. Lake and Mr. Ballance, "Case of Recovery from Temporo-Sphenoidal Abscess." Dr. Beevor and Mr. Ballance, "Case of Removal of Subcortical Cerebral Tumour." Dr. James Taylor and Mr. Ballance, "Case of Trigeminal Neuralgia, in which removal of the Gasserian Ganglion was followed by complete relief."

December 15th, Dr. F. W. Mott, "Changes in the Brain, Muscles, and other Organs, found in persons having died with prolonged epileptiform convulsions." Dr. F. E. Batten, "Congenital Abnormalities in the Nervous Systems of Three Children." Drs. H. H. Tooth and Risien Russell, "Acute Myelitis with Bacteriological Examination."

BALANCE SHEET, 1898.

Cr. NEUROLOGICAL SOCIETY. Dr.

RECEIPTS.

	£	s.	d.
To Balance	46	5	6
Subscriptions for current year	192	4	0
Do. in arrears	12	0	0
Do. in advance	3	0	0
Share of profit on "Brain"	42	3	1
Contributions by Messrs. Macmillan towards cost of illustrations in "Brain"	15	0	0
	£310	12	7

EXPENDITURE.

	£	s.	d.	£	s.	d.
By Stationery and Printing—						
Pulman & Sons	1	15	8			
Bale & Danielsson ...	20	5	9			
				22	1	5
Illustrations—Bale & Danielsson ...				89	7	6
Microscopes—Baker				1	1	0
Hire of Rooms and Refreshments—Medical Society				20	15	0
Messrs. Macmillan for publishing "Brain"...				110	16	6
Petty Cash				0	15	0
Balance				65	16	2
				£310	12	7

Audited and found correct, December 6, 1898,

CHARLES E. BEEVOR, *Hon. Treasurer.*

R. PERCY SMITH.
HENRY HEAD.

RULES.

1.—The Society shall be called the NEUROLOGICAL SOCIETY OF LONDON.

2.—The objects of the Society shall be to promote the advance of Neurology and to facilitate intercourse amongst those who cultivate it, whether from a Psychological, Physiological, Anatomical, or Pathological point of view.

3.—The Society shall consist of Ordinary, Corresponding, and Honorary Members.

4.—Any one engaged in researches bearing on Neurology, or manifesting interest in such researches, shall be eligible for the Ordinary Membership.

5.—Men of distinction in Science, who have contributed to the advancement of Neurology, shall be eligible for the Honorary, or for the Corresponding Membership.

6.—The number of Honorary Members shall be limited to six, and that of Corresponding Members to twelve.

7.—Honorary and Corresponding Members shall have the right of attending the Meetings of the Society and of taking part in them.

8.—Honorary and Corresponding Members shall be elected by the Society on the recommendation of the Council.

9.—Candidates for Ordinary Membership shall be recommended by at least three Members of the Society, who shall append their names to a printed form supplied by the Secretaries to any person seeking Membership.

10.—The Council shall nominate candidates for election into the Society as ordinary Members from among persons so recommended.

11.—The names of Candidates nominated by the Council shall be submitted to the next Meeting of the Society, and shall be balloted for at the next subsequent meeting, one black ball in ten excluding.

12.—The Annual Subscription of an Ordinary Member shall be One Pound, due in advance.

13.—The Treasurer shall send to each Member, shortly before the Annual General Meeting, a notice reminding him that his Subscription becomes due on that day.

14.—Non-payment of the Subscription within twelve months after it is due, shall be considered as equivalent to resignation.

15.—The Council shall consist of a President, two Vice-Presidents, two Secretaries, one Treasurer, and ten Councillors.

16.—Five Members of the Council shall form a quorum.

17.—The office of President shall be tenable for one year, and be entered upon at the beginning of each year by the Senior Vice-President.

18.—The office of Vice-President shall be tenable for two years; one Vice-President being elected every year.

19.—The Secretaries and Treasurer shall be elected annually with eligibility for re-election.

20.—The Councillors shall be elected for one year, and not more than eight shall be eligible for re-election to the same office during the following year.

21.—One full week before the Annual General Meeting, the Secretaries shall send to each Member a balloting paper containing the names of the Officers and Councillors whom the Council nominate for the ensuing year.

22.—The Society shall elect the Council by ballot, each Member, however, being at liberty to substitute other names for any of those upon the list.

23.—There shall be six ordinary meetings annually, of which the first held in each year shall be the Annual General Meeting.

24.—Notices of each meeting, and of the subjects to be considered, shall be sent by the Secretaries to each Member of the Society at least one week before the meeting.

25.—Special Meetings shall be held at the option of the Council, or at the request, in writing, of twenty Members.

26.—The President shall have the power of inviting any person to attend and to take part in the scientific work of the meeting.

27.—If at any time the Council shall be of opinion that the interests of the Society require the expulsion of a Member, they shall submit the question to a special General Meeting, at which, if more than one-half of the Members of the Society vote, by ballot as usual, for the expulsion of the Member, his subscription for the current year shall be returned to him, and he shall thereupon cease to be a Member of the Society.

28.—The Council shall draw up and submit for the approval of the Society, supplementary rules regulating the dates, places, and character of the meetings; shall propose special subjects for investigation by the Society, and shall nominate sub-committees for the methodical carrying out of such investigations. They shall decide, from time to time, on the form of publication which its proceedings are to assume.

29.—No alteration shall be made in the present rules, excepting at the Annual Meeting, or at a Special Meeting convened for the purpose, and unless it be proposed by the Council, or in writing by at least twenty Members, the usual notice be given of the proposed change to every Member before the meeting at which it is to be brought forward.

Each Member receives quarterly, from the beginning of the year in which he is elected, a copy of "BRAIN; a Journal of Neurology," the organ of the Society, and edited for it by A. de Watteville, M.A., M.D., B.Sc.

HONORARY MEMBERS.

Mr. Herbert Spencer, London.
Professor Wundt, Leipzig.
,, Hitzig, Halle.
Sir Samuel Wilks, Bart., London.

CORRESPONDING MEMBERS.

Professor Erb, Heidelberg.
,, Golgi, Pavia.
,, Goltz, Strasburg.
,, Grasset, Montpelier.
,, Jolly, Berlin.
,, Luciani, Rome.
,, Munk, Berlin.
,, Obersteiner, Vienna.
,, Retzius, Gustaf, Stockholm.
,, Ribot, Paris.
Dr. Weir Mitchell, Philadelphia.

LIST OF PRESIDENTS FROM THE FOUNDATION OF THE SOCIETY.

1886 J. Hughlings Jackson, M.D., F.R.S.
1887 Sir Samuel Wilks, Bart., M.D., F.R.S.
1888 Sir James Crichton-Browne, M.D., F.R.S.
1889 Jonathan Hutchinson, F.R.S.
1890 Thomas Buzzard, M.D.
1891 John S. Bristowe, M.D., F.R.S.
1892 Henry C. Bastian, M.D., F.R.S.
1893 Edward A. Schäfer, F.R.S.
1894 David Ferrier, M.D., F.R.S.
1895 Sir William H. Broadbent, Bart., M.D., F.R.S.
1896 Alexander Hill, M.A., M.D.
1897 George H. Savage, M.D.
1898 Victor Horsley, M.B., F.R.C.S., F.R.S.
1899 W. H. Gaskell, M.D., F.R.S.

LIST OF HUGHLINGS JACKSON LECTURERS.

1897 J. Hughlings Jackson, M.D., F.R.S.

*** Members are requested to communicate with the Secretaries when corrections are necessary.

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EXPLANATION OF ABBREVIATIONS.

O.M., Original Member.
Pres., President
V P., Vice-President.
Tr , Treasurer.
Sec , Secretary.
C., Member of Council.
H.J.L., Hughlings Jackson Lecturer.

ORDINARY MEMBERS.

Elected.

1892 Alexander, Robert Reid, M D., The Asylum, Hanwell, W.

1897 Anderson, H Kerr, M.B , B Sc , 9, Park Terrace, Cambridge.

1894 Andriezen, W. Lloyd, M.D.

1891 Ballance, C. A., M.S., F.R.C.S., 106, Harley Street, W. (C., 1897-9.)

O.M. Barlow, Thomas, M.D., F R.C P , 10, Wimpole Street, W.

1897 Barratt, J. O. Wakelin, 26, Upper Wimpole Street, W.

O.M. Bastian, H. Charlton, M.D., F.R.C.P., F.R.S., 8a, Manchester Square, W. (Pres , 1892 ; V.P., 1891 ; C., 1886-9, 1893-5.)

1897 Batten, Frederick E., M.D., M.R.C.P., 124, Harley Street.

O.M. Beach, Fletcher, M.B., F.R.C.P., Winchester House, Kingston Hill, Surrey

„ Beevor, C. E., M.D , F.R.C.P., 33, Harley St., W. (Tr , 1894-9 , C 1893)

1888 Birt, Ernest, M.D., L.R C.P., M R.C S., West Riding Asylum, Wakefield.

1898 Bolton, Joseph Shaw, M.D., B.S., B.Sc., Mason College, Birmingham.

1896 Bond, C. Hubert, M.D , D.Sc.Edin., London County Asylum, Bexley, Kent.

1892 Bowlby, Anthony A., F.R.C.S., 24, Manchester Square, W.

1898 Boyce, Rubert W., M.B.Lond., University College, Liverpool.

„ Boycott, Arthur Norman, M.D.Cantab., Cane Hill Asylum, Purley, Surrey.

„ Bradbury, John B., M.D Cantab., F.R.C P.Lond , 4, St. Peter's Terrace, Cambridge.

1889 Bradford, J. R , M.D , D.Sc., F.R.C P., F.R.S., 60, Wimpole St., W.

O.M. Bramwell, Byrom, M.D , F.R.C.P.Ed., 23, Drumsheugh Gardens, Edinburgh. (C., 1894.)

1895 Bramwell, John Milne, M B., C.M., 2, Henrietta Street, W.

1892 Bristowe, Hubert Carpenter, M.D., L.R.C.P., M.R.C.S., 18, Warwick Road, Maida Vale.

O.M. Broadbent, Sir Wm. H., Bart , M.D., F.R C.P , F.R.S., 84, Brook Street, W. (Pres., 1895 ; V.P., 1893 ; C., 1886-7, 1896.)

Elected

1894 Brodie, T. Gregor, M.D., L.R.C.P., Lindfield, Uxbridge Road, Surbiton.

1897 Brown, H. H., M.D., F.R.C.S., 22, Museum Street, Ipswich.

1888 Brown, Sanger, M.D., 100, State Street, Chicago.

O.M. Bruce, Alex., M.D., F.R.C.P.Ed., 18, Alva Street, Edinburgh. (C. 1895.)

„ Bruce, J. Mitchell, M.D., F.R.C.P., 23, Harley Street, W.

1898 Bruce, Samuel Noble, M.R.C.S.Eng., 43, Kensington Gardens Square.

O.M. Brunton, T. Lauder, M.D., F.R.C.P., F.R.S., 10, Stratford Place, W. (C., 1896-8.)

1895 Bryan, Frederick, M.B.Dunelm, M.R.C.P., The Asylum, New Southgate, N.

„ Bryant, John Henry, M.D.Lond., L.R.C.P., Guy's Hospital, S.E.

1890 Bury, Judson Sykes, M.D., F.R.C.P., 10, St. John Street, Manchester.

O.M. Buzzard, Thomas, M.D., F.R.C.P., 74, Grosvenor Street, W. (Pres., 1890; V.P., 1888-89; C., 1886-7, 1891-5.)

1898 Caley, Albert, M.D.Lond., M.R.C.P., 24, Upper Berkeley Street, W.

1898 Campbell, Harry, M.D., B.S., F.R.C.P.Lond., 23, Wimpole St., W.

1887 Cattell, J. McK., M.A., Ph.D., Columbia College, New York, U.S.A.

1891 Clarke, J. Michell, M.D., F.R.C.P., 28, Pembroke Road, Clifton, Bristol.

1898 Clinch, Thomas Aldous, M.D.Edin., Durham County Asylum, Winterton, Ferryhill, Co. Durham.

O.M. Cobbold, C. S. W., M.D., F.R.C.P.Ed., Bailbrook House, Bath.

1892 Cole, Robert Henry, M.D., M.R.C.P., M.R.C.S., 53, Upper Berkeley Street, Portman Square.

1890 Colman, W. S., M.D., F.R.C.P., 22, Wimpole Street, W. (Sec., 1899.)

„ Corner, Harry, M.D., L.R.C.P., Brook House, Southgate, Middlesex.

1898 Crookshank, F. Graham, M.D.Lond., M.R.C.S., L.R.C.P., County Asylum, Berry Wood, Northampton.

1894 Cuming, James, Prof., M.S., F.R.C.P.I., 33, Wellington Place, Belfast.

1895 Davidson, Andrew, M.B., C.M., The County Asylum, Dorchester, Dorset.

1897 Dawson, William R., M.D., B.Ch., Farnham House, Finglas, Co. Dublin, Ireland.

1894 Dean, H. Percy, M.D., F.R.C.S., 69, Harley Street, W.

1898 Dodd, Henry Work, F.R.C.S.Eng., 136, Harley Street, W.

O.M. Dreschfeld, Julius, M.D., F.R.C.P., 325, Oxford Road, Manchester. (V.P., 1898-9.)

„ Drummond, David, M.D., 6, Saville Place, Newcastle-on-Tyne.

1892 Dupuy, Eugene, M.D., 53, Avenue Montaigne, Paris.

1889 Eccles, A. Symons, M.B., M.R.C.S., 28, Hertford Street, Mayfair, W.

O.M. Ferrier, David, M.D., F.R.C.P., F.R.S., 34, Cavendish Square, W. (Pres., 1894: V.P., 1892-3; C., 1886-90-95.)

Elected

O M. Foster, Michael, M.D., F.R.S., Shelford, Cambridge.

1888 Fox, Arthur, M.B., F.R.C.P.Ed., 16, Gay Street, Bath.

O.M. Fox, E. Long, M.D., F.R.C.P., Church House, Clifton, Gloucestershire.

,, Gaskell, W. H., M.D., F.R.S., The Uplands, Great Shelford, Cambs. (Pres., 1899; V.P., 1897-8; C., 1896.)

,, Gee, Samuel, J., M D., F.R C.P., 31, Upper Brook Street, W.

,, Godlee, R. J., M.B., F.R.C.S., 19, Wimpole Street, W.

1898 Goodliffe, John Henry, M.D.Aberd., County Asylum, Berry Wood, Northampton.

1897 Gossage, Alfred Milne, M.B., M.R.C.P., 54, Upper Berkeley Street.

1892 Gotch, Francis, M A., F.R.S., The Lawn, Banbury Road, Oxford

1893 Grant, Dundas, M D., F.R.C S., 8, Upper Wimpole Street, W.

O.M. Gunn, R., Marcus, M.B., F R C.S., 54, Queen Anne Street, W. (C., 1899.)

1895 Guthrie, Leonard, M.D., M.R.C.P., 15, Upper Berkeley Street, W.

1893 Halliburton, William Dobinson, M.D., F.R.C.P., F.R.S., 9, Ridgemount Gardens, W C.

O M. Hamilton, D. J , M.B , F.R S.E., University, Aberdeen.

1898 Hanbury, William R., M.R.C.S., L R C.P., The Oaks, Longlands Road, Sidcup.

1897 Harris, Wilfred J., M.D., M.R.C.P., 7, Craven Mansions, Craven Terrace, W.

1898 Hartley, W. Darley, M.D. (Dunelm), M.R C.P. (Lond.), "Mayfield," Gilmore Hill Road, Cape Town, South Africa.

,, Haslett, John Handfield, M.R C.S., L.R.C.P., Halliford House, Sunbury-on-Thames.

1891 Hawkins, Herbert Pennell, M.D., F.R.C.P., 56, Portland Place, W.

O.M. Haycraft, J. B., M.B., F.R.S.E , The University, Cardiff.

1891 Head, Henry, M D., M.R.C.P., 61, Wimpole Street, W.

O.M. Hill, Alex , M A., M.D., Downing Lodge, Cambridge. (Pres., 1896; V.P , 1895; C., 1892-94.)

,, Hopkins, John, F.R.C.S., London Sick Asylum, Cleveland Street, W.

,, Horsley, Victor, F R C.S., F.R.S., 25, Cavendish Square, W. (Pres., 1898; V.P., 1896-7; C., 1892-3, 1899.)

1889 Huggard, William R., M.D., F.R.C.P., Davos Platz, Switzerland.

1896 Hulme, George Frederick, M.D., M.S.Ed., Montague Road, Felixstowe.

1889 Humphry, Laurence, M.D., M.R.C P., 8, Trinity Street, Cambridge.

O.M. Hutchinson, Jonathan, F R.C.S., F.R S., 15, Cavendish Square, W. (Pres., 1889; V.P., 1887-88; C., 1886, 1890.)

1889 Hyslop, T. B., M.D., C.M , Bethlem Royal Hospital, Lambeth, S.E.

O.M. Jackson, J. Hughlings, M.D., F.R.C.P., F.R S., 3, Manchester Square, W. (Pres., 1886; H.J.L., 1897; C., 1887-92.)

,, Jessop, W. H., M.B., F R.C.S., 73, Harley Street, W.

1895 Johnston, George, M.D., M.R.C.P., 6, Manchester Square, W.

Elected

1892 Jones, Henry Lewis, M.D., F.R.C.P., 61, Wimpole Street, W.

1894 Jones, Robert, M.D., F.R.C.S., Claybury Asylum, Woodford, Essex.

" Kidd, Percy, M.D., F.R.C.P., 60, Brook Street, W.

1896 Langdon, F. W., M.D., Cincinnati, Ohio, U.S.A.

1898 Langdon-Down, Reginald L., M.B., B.C.Cantab., M.R.C.P.Lond., 81, Harley Street, W.

O.M. Langley, J. N., M.A., D.Sc., F.R.S., Trinity College, Cambridge (C., 1898-9.)

1888 Lawford, J. B., M.D., F.R.C.S., 99, Harley Street, W.

O.M. Lees, D. B., M.D., F.R.C.P., 22, Weymouth Street, W.

1897 Lewis, H. Wolseley, M.R.C.S., L.R.C.P., Claybury Asylum, Woodford, Essex.

" Lowenthal, Max, M.D., M.R.C.P., 84, Princes' Road, Liverpool.

1898 MacCormac, John M'Gee, M.D.Durh., L.R.C.P., L.R.C.S.Edin., 31, Victoria Place, Belfast.

" McAldowie, Alexander M., M.D.Aberd., 6, Brook Street, Stoke-on-Trent.

1891 Macdonald, Peter William, M.D., C.M., The County Asylum, Dorchester, Dorset.

" Mackenzie, Hector William Gavin, M.D., F.R.C.P., 59, Welbeck Street, W.

O.M. Mackenzie, Stephen, M.D., F.R.C.P., 18, Cavendish Square, W. (C., 1896-8.)

1896 Mackintosh, Ashley W., M.A., M.D., Wellington House, Alford Place, Aberdeen.

1889 Macphail, S. R., M.D., Borough Asylum, Rowditch, Derby.

O.M. Maguire, Robert, M.D., F.R.C.P., 4, Seymour Street, W. (Sec., 1890-93; C., 1893-96.)

" Mann, J. Dixon, M.D., F.R.C.P., 16, St. John's Street, Manchester.

1894 Martin, Sidney, M.D., F.R.C.P., F.R.S., 10, Mansfield Street, W.

1893 Maude, Arthur, L.R.C.P., M.R.C.S., Westerham, Kent.

1891 May, W. Page, M.D., M.R.C.P., Helouan, Cairo, Egypt.

1890 Menzies, William Francis, M.D., B.Sc., M.R.C.P., County Asylum, Rainhill, Lancs.

O.M. Mercier, C., M.B., M.R.C.P., Flower House, Southend, Catford, S.E. (C. 1899.)

1897 Meyer, Adolf, M.D., Clark University, Worcester, Mass., U.S.A.

O.M. Mickle, W. Julius, M.D., F.R.C.P., Grove Hall Asylum, Bow, E. (C., 1895-97.)

1895 Moore, Norman, M.D., F.R.C.P., 94, Gloucester Place, W.

O.M. Morris, Malcolm, F.R.C.S.Ed., 8, Harley Street, W.

1888 Mott, F. W., M.D., F.R.C.P., F.R.S., 25, Nottingham Place, W. (Sec., 1894-8; C., 1899.)

1894 Murray, George R., M.A., M.D., F.R.C.P., 11, Ellison Place, Newcastle-on-Tyne.

Elected

1889 Murray, H. Montague, M.D., F.R.C.P., 27, Saville Row, W.

O.M. Nettleship, Edward, F.R.C.S., 5, Wimpole Street, W.
„ Nicolson, David, C.B., M.D., M.R.C.P.Ed., Elmhyrst, Guildford, Surrey.
1888 Niermeyer, J. H. H., M.D., Amsterdam.
„ Norman, Conolly, F.R.C.P.I., F.R.C.S.I., Richmond Asylum, Dublin.

1887 Ogilvie, George, M.B., M.R.C.P., 22, Welbeck Street, W.
„ Ogilvie, Leslie, M.B., M.R.C.P., 46, Welbeck Street, W.
„ Oliver, Thomas, M.D., F.R.C.P., 7, Ellison Place, Newcastle-on-Tyne.
O.M. Orange, Wm., C.B., M.D., F.R.C.P., The Bryn, Godalming, Surrey.
„ Ord, W. M., M.D., F.R.C.P., 37, Upper Brook Street, W. (C., 1893-94.
„ Ormerod, J. A., M.D., F.R.C.P., 25, Upper Wimpole Street, W. (C., 1895-7.)

„ Page, Herbert William, M.A., F.R.C.S., 146, Harley Street, W. (C., 1891-2.)
1895 Parkinson, John Porter, M.D.Lond., M.R.C.P., 40, Wimpole Street, W.
1896 Paterson, Donald Rose, M.D.Edin., M.R.C.P., 18, Windsor Place, Cardiff.
1895 Pinder, George, M.B., B.C., Seafield House, Ramsey, Isle of Man.
1888 Pitt, G. N., M.D., F.R.C.P., 15, Portland Place, W.
O.M. Poore, G. Vivian, M.D., F.R.C.P., 32, Wimpole Street, W. (C., 1898-9.)
O.M. Purves, W. Laidlaw, M.D., 20, Stratford Place, W.

1894 Ransom, William B., M.D., F.R.C.P., The Pavement, Nottingham.
1890 Rayner, Henry, M.D., M.R.C.P.Ed., 2, Harley Street, W.
O.M. Reid, E. W., M.B., University College, Dundee.
1897 Reissmann, Charles H., B.A., B.Sc., Saxony Villas, Oppidans Road, Primrose Hill.
1893 Rennie, George E., M.D.
1895 Reynolds, Ernest S., M.D., F.R.C.P., 23, St. John Street, Manchester.
1892 Richards, Joseph Peeke, M.R.C.S., 6, Freeland Road, Ealing, W.
1891 Rivers, W. H. R., M.A., M.D., M.R.C.P., St. John's College, Cambridge. (C. 1897-8.)
1898 Robertson, William Ford, M.D., C.M.Edin., 12, Bristo Place, Edinburgh.
1892 Rowe, Edmund Lewis, L.R.C.P., L.R.C.S., Borough Asylum, Ipswich.
„ Ruffer, Marc Armand, M.D., Cairo.
1889 Russell, J. S. Risien, M.D., F.R.C.P., 4, Queen Anne Street, W. (Sec., 1896-9.)

O.M. Sanderson, J. Burdon, M.D., F.R.C.P., F.R.S., Banbury Road, Oxford.
„ Savage, G. H., M.D., F.R.C.P., 3, Henrietta Street, Cavendish Square, (Pres., 1897; V.P., 1895; C., 1886-90, 1898.)

Elected

1888 Savill, T. D., M.D., M.R.C.P., 60, Upper Berkeley Street, W.

O.M. Schafer, E. A., F.R.S., University College, Gower Street. (Pres., 1893; V.P., 1892; C., 1886-90.)

,, Semon, Sir Felix, M.D., F.R.C.P., 39, Wimpole Street, W. (C., 1899.)

1898 Seward, Wm. Joseph, M.B.Lond., Colney Hatch Asylum, N.

O.M. Sharkey, S. J., M.D., F.R.C.P., 22, Harley Street, W. (C., 1889-92.)

,, Sherrington, C. S., M.D., F.R.S., 16, Grove Park, Liverpool. (C. 1892-95.)

1894 Shuttleworth, George E., M.D., Ancaster House, Richmond.

1898 Simpson, Francis O., L.R.C.P.Lond., M.R.C.S.Eng., Hawkhead Asylum, Paisley, Scotland.

1895 Smith, F. J., M.D., M.R.C.P., 4, Christopher Street, Finsbury Square, E.C.

1887 Smith, R. Percy, M.D., F.R.C.P., 86, Queen Anne Street, W.

1895 Smith, Telford, M.D., B.S., Royal Albert Asylum, Lancaster.

,, Spicer, William T. H., M.D.Cantab., F.R.C.S., 47, Welbeck Street, W.

,, Stansfield, Thos. E. K., M.B., Claybury Asylum, Woodford, Essex.

,, Stanley, Douglas, M.D.Edin., 9, Easy Row, Birmingham.

1892 Starling, Ernest Henry, M.D., F.R.C.P., B.S., 8, Park Square, N.W.

1897 Stewart, Purves, M.A., M.D., M.R.C.P., 139, Harley Street, W.

O.M. Stewart, Sir T. Grainger, M.D., F.R.C.P.Ed., 19, Charlotte Square, Edinburgh.

,, Stirling, Wm., M.D., D.Sc., Owens College, Manchester.

1897 Stoddart, Wm. H., M.D., B.S., M.R.C.P.Lond., Bethlem Royal Hospital, Lambeth, S.E.

1895 Stout, G. F., M.A., St. John's College, Cambridge.

1887 Suckling, C. W., M.D., M.R.C.P., 103, Newhall Street, Birmingham.

O.M. Sully, James, M.A., LL.D., 1, Portland Villas, Hampstead. (V.P., 1890-91.)

1889 Sutherland, Henry, M.D., M.R.C.P., 21, New Cavendish Street, Portland Place, W.

1888 Sykes, Henry W., M.D., M.R.C.P., 4, Oxford and Cambridge Mansions, Hyde Park, W.

1898 Taylor, F. R. P., M.D., B.S.Lond., Darenth Asylums and Schools, Dartford, Kent.

1891 Taylor, James, M.D., F.R.C.P., 49, Welbeck Street, W.

1898 Thomson, H. Campbell, M.D., M.R.C.P., 34, Queen Anne Street, W.

1889 Thorburn, Wm., F.R.C.S., The Limes, Nelson Street, Manchester.

1892 Titchener, E. B., B.A., Ph.D., 72, Heustis Street, Ithaca, N.Y.

O.M. Tooth, H. H., M.D., F.R.C.P., 34, Harley Street, W. (Sec., 1891-95; C., 1896-9.)

1892 Trevelyan, E. F., M.D., B.Sc., M.R.C.P., 40, Park Square, Leeds.

1892 Tuckey, Charles Lloyd, M.D., C.M., 88, Park Street, Grosvenor Square, W.

1892 Tuke, Sir J. Batty, M.D., F.R.C.P.Ed., 20, Charlotte Sq., Edinburgh.

Elected

1891 Tuke, Thomas Seymour, M.B., M.R.C.S., Chiswick House, Chiswick.

,, Turner, William Aldren, M.D., F.R.C.P., 13, Queen Anne Street, W.

1898 Turney, Horace G., M.B., M.Ch.Oxon, F.R.C.P.Lond., 68, Portland Place, W.

O.M. Tweedy, John, F.R.C.S., 100, Harley Street, W.

1888 Voorthus, J. A., M.D., Apeldoorn, 542, Loulaan, Netherlands.

1895 Wade, Arthur L., M.D., Somerset and Bath Asylum, Wells.

1894 Walker, A. Stodart, M.B., 30, Walker Street, Edinburgh.

O.M. Waller, Augustus, M.D., F.R.S., 16, Grove End Road, N.W. (V.P., 1899; C., 1894-7.)

O.M. Ward, J., D.Sc., Trinity College, Cambridge.

,, Warner, Francis, M.D., F.R.C.P., 5, Prince of Wales Terrace, Kensington Palace, W.

1892 Washbourn, J. W., M.D., F.R.C.P., 6, Cavendish Place, W.

O.M. Watteville, A. de, M.A., M.D., B.Sc., 30, Welbeck Street, W. (C., 1890-95, 1896-9, Sec., 1886-9; Editor of *Brain*.)

1897 Weber, F. Parkes, M.D., F.R.C.P., 19, Harley Street, W.

,, West, Samuel, M.D. F.R.C.P., 15, Wimpole Street, W.

,, White, Ernest W., M.B., M.R.C.P., City of London Asylum, Dartford.

O.M. White, W. Hale, M.D., F.R.C.P., 65, Harley Street, W. (C., 1897-9.)

1894 Whiting, Arthur J., M.D., M.R.C.P., 142, Harley Street, W.

1889 Wiglesworth, Joseph, M.D., F.R.C.P., County Asylum, Rainhill, Lancashire.

1894 Williamson, Richard T., M.D., M.R.C.P., 294, Oxford Road, Manchester.

1896 Wilson, Albert, M.D.Edin., M.R.C.P., 33, Fairlop Road, Leytonstone.

,, Wood, Guy M., M.B., M.R.C.P., County Asylum, Rainhill, Lancashire.

1889 Wood, T. Outterson, M.D., M.R.C.P., 40, Margaret Street, Cavendish Square, W.

1892 Woodhead, G. Sims, M.D., F.R.C.P.Ed., Examination Hall, Victoria Embankment.

1898 Young, Robert Arthur, M.D., B.Sc., M.R.C.P., 41, Wimpole St., W.